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Photolariats: synthesis, metal ion complexation and photochromism

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Photolariat development, as an extension to the family of synthetic photochromic crown ether receptors, or photocrowns, is reported. Incorporated additional chelating groups, namely two anisoles or thioanisoles, contribute in completing the metal ion coordination sphere with different affinities and selectivities for a range of ions. Single crystal X ray diffraction analysis suggests that the thermally stable \textit{trans} form of the receptor is unsuitable for ion binding, consistent with spectrophotometric and NMR titration results, which is largely improved in the \textit{cis} form as the basis for the photocontrolled ion coordination/ejection. In terms of the azobenzene containing receptor photochemistry, a photostationary state highly enriched in the \textit{cis} form (94:6, \textit{cis}/\textit{trans}) is reached, with slow thermal return ($1.1 \times 10^{-5}$ s\textsuperscript{-1}) in the dark, which can undergo multiple cycles without discernable photodegradation.

Keywords: photolariat; azobenzene; macrocycles; receptor; photochromism

1. Introduction

A wealth of synthetic macrocyclic receptors have been reported over the last 30 40 years, which have shown varying affinities to a wealth of guests, notably metal ions (1, 2). Among these receptors, stimulus-modulated species where the binding affinity can be modified as a response to a signal represents an expanding research area. This is due to the scope of potential applications in biomimetic nanotechnology as well as molecular biology, where liberation (or uptake) of a chemical effector at a given time is employed to ultimately allow elucidation of specific biological pathways (3, 4). In this context, photoactive receptors are particularly attractive as light energy can be applied to autonomous molecules in solution with high spatial and temporal resolution (5). Increasingly popular two photon absorption techniques offer a further possibility to irradiate with NIR light in the so-called therapeutic window, allowing deeper penetration of excitation light to activate deep lying molecules (6). Reversible photinduced ion release and uptake imply photochromic receptors, where light switching between two distinct forms has a direct influence on binding. Indeed, a wealth of photochromes have been integrated with different receptors to give access to photocontrolled binding of a range of species (7, 8). The origin of the binding change is due to either electronic or steric effects. In the former case, on switching, electron density is less available to binding sites in one form with respect to the other, with a concomitant lowered binding constant. For the latter scenario, steric effects come into play when there is a significant geometrical change in the photoactive group between each form of the photochrome, which varies the shape of the receptor and hence suitability to bind a guest species. A popular choice of photochrome is azobenzene, which can be efficiently and reversibly switched from the thermally stable elongated \textit{trans}-form to the more compact \textit{cis}-form on UV irradiation. The return \textit{cis}-to-\textit{trans} transformation can be achieved thermally or by visible irradiation. In this way, different hosts such as cavitands and capsules can be rendered photoactive and more specifically the miniscule internal (yoctolitre) spaces available for chemical encapsulation can be controlled, which can ultimately lead to recognition, sequestration and reactivity of small molecules, depending on the host (9, 10). Among different manifestations of azobenzene in supramolecular hosts, one of the most successful implementations was the development of photocrowns where an azobenzene unit was directly incorporated in the macrocyclic host or in ‘butterfly’ variants (7, 11 15). However, binding constants are typically reasonably low and strategies to increase this parameter would be anticipated to widen the scope of implementation of these photoactive functional molecules. Concerning the photoswitching and photochemistry of these macrocyclic azobenzene-containing hosts, the complexing ring imparts differing levels of strain on the azobenzene link, which as a
function of size can drastically modify quantum yields, activation energy of cis-to-trans interconversion, absorption band intensities, as well as complexation selectivities (16 19). As part of our ongoing work in the area of photocontrolled receptors and functional molecules and assemblies, we report herein the synthesis, photochemistry and complexation properties of lariat ethers, which incorporate a photoswitching azobenzene unit, deemed photolariats. The structural formulae of two members of this family are shown in Figure 1. In addition to the complexing heteroatom set of the macrocycle, two additional complexing atoms, oxygen and sulphur (1a and 1b, respectively), are added. Para- as opposed to ortho-substitution of the azobenzene with respect to the central nitrogens may be anticipated to amplify the geometrical difference between cis-form and trans-form, consequently changing the binding properties and photochromism.

2. Experimental

2.1. Materials and methods

Commercially available starting materials were obtained from Aldrich, AlfaAesar, Lancaster or Avocado. Compounds 2 (20) and 4 (21) were synthesised according to literature procedures. Anhydrous absolute ethanol and dimethylformamide (DMF) solvents were used as received. Dichloromethane and pyridine were distilled over calcium hydride (CaH₂) immediately before use. Tetrahydrofuran (THF) was dried over sodium/benzophenone and distilled immediately before use. Nuclear magnetic resonance (NMR): the ¹H and ¹³C NMR spectra were recorded on a Bruker DPX200 (¹H: 200 MHz) or a Bruker Avance 300 (¹H: 300 MHz; ¹³C: 75 MHz) spectrometer. Chemical shifts (δ) are expressed relative to tetramethylsilane (TMS) using the residual signals of the deuterated solvents (CDCl₃, d₆-DMSO) as an internal reference. The coupling constants are calculated in Hertz (Hz). For the assignment of signals, the following abbreviations are used: s singlet, d doublet, t triplet, q quartet, dd doublet of doublets and m multiplet. Mass spectrometry: the mass spectra were recorded by the Centre of Study and Structural Analysis Organic Molecules at the University of Bordeaux, France. Electrospray ionisation (ESI) mass spectra were performed on a QStar Elite mass spectrometer (Applied Biosystems). The instrument is equipped with an ESI source and spectra were recorded in the positive mode. The electrospray needle was maintained at 5000 V and operated at room temperature. Samples were introduced by injection through a 20 µL sample loop into a 4500 µL/min flow of methanol from the LC pump. MALDI-MS spectra were performed on a Voyager mass spectrometer (Applied Biosystems). The instrument is equipped with a pulsed N₂ laser (337 nm) and a time-delayed extracted ion source. Spectra were recorded in the positive-ion mode using the reflectron and with an accelerating voltage of 20 kV. A dithranol matrix solution was employed. GC/MS mass spectra were performed on a Trace GC 2000 gas chromatograph equipped with a RTX5 MS column (length 15 m; diameter 0.25 mm; film 0.25 µm), coupled to a Thermofinnigan Trace electron impact (EI) mass spectrometer. Samples were measured using a source temperature of 200°C and a 150 µA ionisation current. Electronic absorption spectroscopy: the electronic absorption spectra were recorded on optically dilute solutions in 1 cm pathlength quartz cells, whose temperature was thermostated, using a double beam Varian Cary 5000 UV vis-NIR spectrophotometer. Photoirradiation systems: irradiations at 365 nm were performed with a portable Fisher Bioblock mercury lamp (type thin layer chromatography (TLC)) with a power of 2 × 6 Watts. Isomerisation quantum yields were determined using stirred standard solutions irradiating at 334 or 365 nm with a mercury xenon lamp equipped with a monochromator. A ferrioxalate actinometer was employed following the Hatchard and Parker method (22). Photoisomerisation (trans-to-cis) of 1a and 1b was performed at 365 nm while parent azobenzene isomerisation was achieved at 334 nm because of the differences in the electronic

![Figure 1](image-url)

Figure 1. Photoswitching of prototype photolariats 1a (X = O) and 1b (X = S). E isomers should weakly complex with cations, while the Z isomer is anticipated to be better adapted to complex.
absorption spectra. The appropriate actinometer quantum yield value was used in each case and correction was made for incomplete light absorption (22). All irradiation samples were air-equilibrated.

Single-crystal X-ray diffraction analysis: 1a: summary of data CCDC 864623: formula: C_{24}H_{24}N_{2}O_{4}S_{2}; unit cell parameters: a 14.5845 (5), b 11.8355 (4), c 22.7467 (8), β 97.576 (2); space group C2/c; crystal data: (C_{24}H_{24}N_{2}O_{4}S_{2}), M 762.88, T 213(2) K, monoclinic, space group C2/c, α 14.5845 (5), b 11.8355 (4), c 22.7467 (8) Å, β 97.576 (2), V 3892.1 (2) Å³, Dc 1.302 g cm⁻³, Z 4, F(000) 1624, 17,692 reflections measured, 2195 independent reflections (R_{int} 0.049), refinement on F² against all reflections. The weighted R-factor wR and goodness of fit GOF are based on F², GOF 1.09, R(F² > 2σ(F²)) 0.085, wR(F²) 0.259. Hydrogen site location was inferred from neighbouring sites, H-atom parameters constrained, 949 reflections used for refinement, 254 parameters and no restraint. The data collection was performed on a Bruker microstar rotating anode at the Cu Kα wavelength; cell refinement and data reduction were computed with the Bruker suite X8 Proteum; SHELXD97 (Sheldrick, 2008) was used to solve the crystal structure and SHELXL97 (Sheldrick, 1997) for refinement.

5a: Summary of data CCDC 864624: crystal data: (C_{24}H_{24}N_{2}O_{4}S_{2}), M 468.47, T 213 (2) K, orthorhombic, space group Pca, α 16.4963 (8), b 17.9052 (9), c 7.1865 (4) Å, V 2122.67 (19) Å³, Dc 1.366 g cm⁻³, Z 4, F(000) 920, 10,641 reflections measured, 949 independent reflections (R_{int} 0.035), refinement on F² against all reflections. The weighted R-factor wR and goodness of fit GOF are based on F², GOF 1.33, R(F² > 2σ(F²)) 0.04, wR(F²) 0.115. Hydrogen site location was inferred from neighbouring sites, H-atom parameters constrained, 147 parameters and no restraint. The data collection has been performed on a Bruker microstar rotating anode at the Cu Kα wavelength; cell refinement and data reduction were computed with the Bruker suite X8 Proteum; SHELXD97 (Sheldrick, 2008) was used to solve the crystal structure and SHELXL97 (Sheldrick, 1997) for refinement.

5b: Summary of data CCDC 864625: crystal data: (C_{24}H_{24}N_{2}O_{4}S_{2}), M 468.47, T 213 (2) K, triclinic, space group P-1, a 4.702 (6), b 13.869 (5), c 18.607 (8) Å, α 109.90°, β 90.06°, γ 99.33°, V 1123.8 (2) Å³, Dc 1.385 g cm⁻³, Z 2, F(000) 492, 3155 reflections measured, 2340 independent reflections (R_{int} 0.223), refinement on F² against all reflections. The weighted R-factor wR and goodness of fit GOF are based on F², GOF 0.656, R(F² > 2σ(F²)) 0.16, wR(F²) 0.36. Hydrogen site location was inferred from neighbouring sites, H-atom parameters constrained, 5345 reflections used for refinement, 239 parameters and 17 restraints. Data collection was performed on a Rigaku MM07 rotating anode at the Cu Kα wavelength. The CrystalClear (Rigaku/MSC Inc., 2006) suite was used for cell refinement and data reduction; SUPERFLIP (Palatinus, 2007) solved the structure that has been refined using SHELXL97 (Sheldrick, 1997); The WinGX (Farrugia, 1999) software was used to prepare material for publication. It has to be noted that it was not possible to collect better data on these tiny and X-ray sensitive crystals.

2.2. Synthesis procedures

Structural formulae of molecules 1a 9b are shown in Figure 2.

3: To a solution of 2 (657 mg, 2.92 mmol) in DCM (70 mL) were added thionyl chloride (1.52 mL, 20.9 mmol) and triethylamine (0.42 mL, 3.0 mmol) at 0°C. The mixture was refluxed for 2 h. The reaction mixture was concentrated in vacuo and was used in coupling reactions with 6a or 6b without further purification.

5a: A mixture of 4 (2.00 g, 8.85 mmol), thionyl chloride (8.8 mL) and triethylamine (1.8 mL) in DCM (300 mL) was refluxed for 3 h. The solvent and excess thionyl chloride were removed in vacuo, yielding the diacid chloride as a light brown solid. To a well-stirred solution of this diacid chloride (8.85 mmol) in DCM (150 mL), a solution of o-anisidine (2.03 mL, 18 mmol) and triethylamine (2.47 mL, 17.7 mmol) in DCM (150 mL) was added dropwise. The reaction mixture was stirred at room temperature for 6 h and was then washed with water (3 x 100 mL) to remove the triethy lammonium chloride and dried over MgSO₄. The solvent was removed in vacuo and the residue was purified by column chromatography (silica, pentane/ethyl acetate, 7/3, v/v). The obtained product was further purified by recrystallisation from methanol, yielding 5a (2.37 g, 61%). ¹H NMR (CDCl₃, 300 MHz, TMS): δ 9.21 (s, 2H, NH); 8.43 (d, J 7.9 Hz, 2H, CH₂); 7.00 (m, 8H, C HAr); 6.59 (d, J 7.9 Hz, 2H, CH₂); 4.72 (s, 4H, CH₂); 3.46 (s, 6H, CH₃) ppm. ¹³C NMR (CDCl₃, 75 MHz, TMS): δ 165.9; 148.3; 147.2; 126.8; 124.5; 123.0; 120.9; 110.4; 68.5; 55.5. GC/MS (EI): m/z 436.2 (24%, M⁺), 122.9 (100%).

5b: The sulphur analogue 5b (9.74 g, 74%) was obtained similarly to 5a using 2-(methylthio)aniline. ¹H NMR (CDCl₃, 300 MHz, TMS): δ 9.54 (s, 2H, NH); 8.34 (d, J 8.2 Hz, 2H, CH₂); 7.37 (d, J 7.8 Hz, 2H, CH₂); 7.28 (d, J 8.0 Hz, 2H, CH₂); 7.07 (d, J 7.5 Hz, 2H, CH₂); 7.02 (s, 4H, CH₂); 4.76 (s, 4H, CH₂); 2.14 (s, 6H, CH₃) ppm. ¹³C NMR (CDCl₃, 75 MHz, TMS): δ 166.6; 147.6; 137.7; 132.5; 128.7; 126.6; 125.2; 123.4; 120.9; 114.9; 69.2; 18.5 ppm. MS (ESI): m/z 469.1 (M + H⁺); 491.1 (M + Na⁺).

6a: To a solution of diamine 5a (2.06 g, 4.73 mmol) in THF (350 mL), a solution of BH₃ in THF (1 M; 47 mL, 47 mmol) was added dropwise. The mixture was refluxed for 65 h, and the reaction was monitored by TLC (pentane/ethyl acetate, 7/3, v/v). Water (10 mL) was
added to slow down $H_2$ evolution and solvents were evaporated in vacuo. The resulting white solid was used without further purification. The crude product was dissolved in THF (200 mL), and TFA (17.8 mL, 0.24 mol) was added dropwise. The solution was then refluxed for 1 h. THF was evaporated, and an aqueous solution of sodium hydroxide was added to neutralise the reaction mixture. After extraction with DCM, the organic phase was dried over MgSO$_4$. The solvent was evaporated in vacuo, and the residue was purified by chromatography (silica gel, pentane/ethyl acetate, 8/2, v/v) to afford diamine $6a$ (1.56 g, 81%) as a solid. $^1$H NMR (CDCl$_3$, 300 MHz, TMS): $\delta$ 6.66 (m, 12H, $CH_Ar$); 4.78 (s, 2H, $NH$); 4.24 (t, 4H, $CH_2O$); 3.78 (s, 6H, $CH_2O$); 3.57 (t, 4H, $CH_2N$) ppm. $^{13}$C NMR (CDCl$_3$, 75 MHz, TMS): $\delta$ 149.0; 147.1; 137.9; 121.9; 121.2; 116.7; 115.3; 109.9; 109.5; 68.2; 55.3; 43.0 ppm. GC/MS (EI): $m/z$ 408.2 (M$^+$); 135.9.

$6b$: The sulphur analogue $6b$ (1.96 g, 90%) was obtained similarly to $6a$ using $5b$. $^1$H NMR (CDCl$_3$, 300 MHz, TMS): $\delta$ 7.36 (d, $J$ 8.1 Hz, 2H, $CH_Ar$); 7.16 (t, $J$ 7.5 Hz, 2H, $CH_Ar$); 6.92 (m, 4H, $CH_Ar$); 6.62 6.67 (m, 4H, $CH_Ar$); 5.37 (s, 2H, $NH$); 4.24 (t, $J$ 5.7 Hz, 4H, $CH_2O$); 3.59 (t, $J$ 5.9 Hz, 4H, $CH_2N$); 2.25 (s, 6H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 149.2; 148.0; 134.0; 129.4; 122.2; 120.7; 117.8; 115.4; 110.4; 68.2; 43.5; 18.1 ppm. MS (ESI): $m/z$ 441.1675 (M$^+$ + H$^+$); 463.1491 (M$^+$ + Na$^+$); calculated C$_{24}$H$_{28}$N$_2$O$_2$S$_2$Na: 463.1484.

$7a$: To a solution of $3$ (0.76 g, 2.92 mmol, 4 eq.) in DCM (50 mL), triethylamine (0.4 mL) was added dropwise at 0°C and $7a$ (0.27 g, 0.65 mmol, 1 eq.) was subsequently introduced dropwise at room temperature. This mixture was stirred for 22 h, diluted in DCM and washed with a saturated aqueous solution of NaCl (200 mL) and water (200 mL). The crude product was purified by chromatography (silica gel, ethyl acetate/pentane, 7/3, v/v) yielding $7a$ (487 mg, 87%). $^1$H NMR (CDCl$_3$, 300 MHz, TMS): $\delta$ 8.16 (d, $J$ 9.3 Hz, 4H, $CH_Ar$); 7.35 7.23 (m, 4H, $CH_Ar$); 6.94 (m, 4H, $CH_Ar$); 6.91 (d, $J$ 9.3 Hz, 4H, $CH_Ar$); 6.84 (m, 4H, $CH_Ar$); 4.22 3.86 (m, 20H, $CH_2$); 3.77 (s, 6H, $CH_3$) ppm. $^{13}$C NMR
and the reaction mixture was stirred for an additional 60 h at 100 °C. Iodoethoxyethoxy-4-nitrobenzene (0.81 g, 2.40 mmol) was added, and the reaction mixture was stirred for 20 h at 100 °C. The solvent was removed in vacuo. The residue was dissolved in water, and the reaction mixture was neutralised with an aqueous solution of sodium hydroxide. After extraction with DCM, the organic phase was further purified by silica gel chromatography (petroleum ether/ethyl acetate, 1/4, v/v) affording diamine 8a (52 mg, 13%).

Method B. To a solution of diamine 7a (1.00 g, 1.17 mmol) in THF (60 mL), a solution of BH₃ in THF (1 M; 12 mL, 12 mmol) was added dropwise. The mixture was refluxed for 15 h and was filtered hot over a pad of Celite, and the filtrate was evaporated in vacuo. The reaction is quantitative and further purification proved unnecessary. ¹H NMR (CDCl₃, 300 MHz, TMS): δ 7.08 (d, J 7.8 Hz, 2H, CH₃); 6.97 (t, J 7.8 Hz, 2H, CH₃); 6.85 (t, J 7.8 Hz, 4H, CH₃); 6.80 (s, 4H, CH₃); 6.71 (d, J 9 Hz, 4H, CH₃); 6.59 (d, J 9 Hz, 4H, CH₃); 4.05 (t, J 6.9 Hz, 4H, CH₂); 3.95 (t, J 5.1 Hz, 4H, CH₂); 3.81 (s, 6H, CH₃); 3.69 (t, J 5.1 Hz, 4H, CH₂); 3.65 (m, 8H, CH₂); 3.49 (t, J 5.7 Hz, 4H, CH₂) ppm. ¹³C NMR (CDCl₃, 75 MHz, TMS): δ 153.5; 148.7; 141.6; 137.8; 125.8; 124.5; 124.2; 123.8; 121.1; 114.6; 113.8; 70.0; 69.0; 68.2; 67.3; 53.9; 53.4; 14.2 ppm. HRMS (ESI): m/z 881.2832 (M + Na⁺); calculated C₂₃H₃₀N₄·O₁₀S₂·Na: 881.2860.

9a: To a suspension of 10% palladium on charcoal (53 mg) in ethanol (15 mL), 8a (200 mg, 0.24 mmol) and hydrazine hydrate (1.5 mL, 30.9 mmol) were added. The mixture was refluxed for 15 h and monitored by TLC (AcOEt/petroleum ether, 3/2, v/v). The solution was filtered hot over a pad of Celite, and the filtrate was evaporated in vacuo. The sulphur analogue 9a (18%) was obtained similarly to 8a (Method B) using 7b. ¹H NMR (CDCl₃, 300 MHz, TMS): δ 8.14 (d, J 9.2 Hz, 4H, CH₃); 7.22 (d, J 8.1 Hz, 2H, CH₃); 7.02 7.11 (m, 6H, CH₃); 6.90 (d, J 9.6 Hz, 4H, CH₃); 6.81 (s, 4H, CH₃); 4.11 (t, J 4.5 Hz, 4H, CH₂); 4.02 (t, J 6.6 Hz, 4H, CH₂); 3.76 (t, J 4.5 Hz, 4H, CH₂); 3.61 (t, J 6.3 Hz, 4H, CH₂); 3.51 (t, J 6.6 Hz, 4H, CH₂); 3.41 (t, J 6.0 Hz, 4H, CH₂); 2.35 (s, 6H, CH₃) ppm. ¹³C NMR (CDCl₃, 75 MHz, TMS): δ 161.9; 148.7; 141.6; 137.8; 125.8; 124.5; 124.2; 123.8; 121.1; 114.6; 113.8; 70.0; 69.0; 68.2; 67.3; 53.9; 53.4; 14.2 ppm. HRMS (ESI): m/z 877.4 (M + Na⁺); calculated C₂₃H₃₀N₄·O₁₀S₂·Na: 877.4.
1H NMR (CDCl$_3$, 300 MHz, TMS): $\delta$ 7.77 (d, $J$ 9 Hz, 4H, CH$_2$)$_2$; 7.12 (d, $J$ 9 Hz, 4H, CH$_2$)$_2$; 6.93 (m, 4H, CH$_2$)$_2$; 6.67 $-$ 6.85 (m, 8H, C$_{HAr}$); 4.37 (t, $J$ 3.9 Hz, 4H, CH$_2$)$_2$; 3.81 (t, $J$ 8.4 Hz, 4H, CH$_2$)$_2$; 3.78 (s, 6H, CH$_3$)$_2$; 3.70 (t, $J$ 4.2 Hz, 4H, CH$_2$)$_2$; 3.39 (t, $J$ 7.5 Hz, 4H, CH$_2$)$_2$; 3.14 (t, $J$ 8.1 Hz, 4H, CH$_2$)$_2$; 3.08 (t, $J$ 8.0 Hz, 4H, CH$_2$)$_2$; 3.06 (t, $J$ 8.0 Hz, 4H, CH$_2$)$_2$; 3.03 (t, $J$ 8.1 Hz, 4H, CH$_2$)$_2$; 2.99 (t, $J$ 6.3 Hz, 4H, CH$_2$)$_2$; 2.33 (s, 6H, CH$_3$)$_2$ ppm. $^{13}$C NMR (CDCl$_3$, 75 MHz, TMS): $\delta$ 161.1; 153.9; 148.5; 147.3; 138.6; 124.2; 123.4; 122.2; 120.8; 116.4; 114.7; 113.3; 112.0; 70.0; 69.7; 68.2; 66.3; 55.5; 52.9; 29.8 ppm. HRMS (ESI): m/z 763.3711 (M + H$^+$); calculated C$_{44}$H$_{56}$N$_4$O$_6$Na: 823.3533.

The secondary amines resulting from the reduction of the amides 7a and 7b were obtained analogously to 1a using 9b. $^1$H NMR (CDCl$_3$, 300 MHz, TMS): $\delta$ 8.10 (d, $J$ 8.7 Hz, 4H, CH$_2$)$_2$; 7.12 (d, $J$ 9 Hz, 4H, CH$_2$)$_2$; 7.00 (m, 8H, CH$_2$)$_2$; 6.68 $-$ 6.79 (m, 4H, CH$_2$)$_2$; 4.37 (t, $J$ 3.9 Hz, 4H, CH$_2$)$_2$; 3.82 (t, $J$ 8.4 Hz, 4H, CH$_2$)$_2$; 3.37 (t, $J$ 6.3 Hz, 4H, CH$_2$)$_2$; 3.13 (t, $J$ 8.1 Hz, 4H, CH$_2$)$_2$; 2.99 (t, $J$ 6.3 Hz, 4H, CH$_2$)$_2$; 2.33 (s, 6H, CH$_3$)$_2$ ppm. $^{13}$C NMR (CDCl$_3$, 75 MHz, TMS): $\delta$ 161.1; 148.4; 147.3; 147.0; 138.3; 125.5; 124.5; 124.1; 124.0; 123.7; 120.7; 116.3; 113.4; 70.8; 69.5; 68.1; 66.3; 54.0; 54.0; 14.2 ppm. HRMS (ESI): m/z 785.3527 (M + Na$^+$); calculated C$_{44}$H$_{50}$N$_4$O$_6$NaS$_2$: 837.3533.

1a: A pyridine solution (60 mL) of diamine 9a (66 mg, 0.086 mmol) and CuCl (65 mg, 0.66 mmol) was stirred in the dark under air for 20 h at room temperature, and the solvent was then evaporated. The residue was purified by chromatography (silica gel, petroleum ether/ethyl acetate 1:1, v/v) affording azolariat 1a (23 mg, 35%). $^1$H NMR (CDCl$_3$, 300 MHz, TMS): $\delta$ 7.75 (d, $J$ 9 Hz, 4H, CH$_2$)$_2$; 7.12 (d, $J$ 9 Hz, 4H, CH$_2$)$_2$; 6.93 (m, 4H, CH$_2$)$_2$; 6.67 $-$ 6.85 (m, 8H, C$_{HAr}$); 4.37 (t, $J$ 3.9 Hz, 4H, CH$_2$)$_2$; 3.81 (t, $J$ 8.4 Hz, 4H, CH$_2$)$_2$; 3.78 (s, 6H, CH$_3$)$_2$; 3.70 (t, $J$ 4.2 Hz, 4H, CH$_2$)$_2$; 3.39 (t, $J$ 7.5 Hz, 4H, CH$_2$)$_2$; 3.14 (t, $J$ 5.7 Hz, 4H, CH$_2$)$_2$ ppm. $^{13}$C NMR (CDCl$_3$, 75 MHz, TMS): $\delta$ 161.1; 153.9; 148.5; 147.3; 138.6; 124.2; 123.4; 122.2; 120.8; 116.4; 114.7; 113.3; 112.0; 70.0; 69.7; 68.2; 66.3; 55.5; 52.9; 29.8 ppm. HRMS (ESI): m/z 763.3701 (M + Na$^+$); calculated C$_{44}$H$_{51}$N$_4$O$_8$: 763.3701.

1b: The sulphur analogue 1b (32 mg, 21%) was obtained analogously to 1a using 9b. $^1$H NMR (CDCl$_3$, 300 MHz, TMS): $\delta$ 7.77 (d, $J$ 9 Hz, 4H, CH$_2$)$_2$; 7.12 (d, $J$ 9 Hz, 4H, CH$_2$)$_2$; 7.00 (m, 8H, CH$_2$)$_2$; 6.68 $-$ 6.79 (m, 4H, CH$_2$)$_2$; 4.37 (t, $J$ 3.9 Hz, 4H, CH$_2$)$_2$; 3.82 (t, $J$ 8.4 Hz, 4H, CH$_2$)$_2$; 3.37 (t, $J$ 6.3 Hz, 4H, CH$_2$)$_2$; 3.13 (t, $J$ 8.1 Hz, 4H, CH$_2$)$_2$; 2.99 (t, $J$ 6.3 Hz, 4H, CH$_2$)$_2$; 2.33 (s, 6H, CH$_3$)$_2$ ppm. $^{13}$C NMR (CDCl$_3$, 75 MHz, TMS): $\delta$ 161.1; 148.4; 147.3; 147.0; 138.3; 125.5; 124.5; 124.1; 124.0; 123.7; 120.7; 116.3; 113.4; 70.8; 69.5; 68.1; 66.3; 54.0; 54.0; 14.2 ppm. HRMS (ESI): m/z 817.3059 (M + Na$^+$); calculated C$_{44}$H$_{56}$N$_4$O$_6$NaS$_2$: 817.3064 (M + Na$^+$).
cation inside this cavity should be disfavoured. On the other hand, the less elongated cis-form may be anticipated to have a less drastic effect on the binding site. Indeed, molecular modelling suggests that 1a-Z adopts a more globular shape, which is conducive with complexation. (Due to the low energy barrier for single C-C bond rotation, one definitive structural orientation is not shown.)

Additionally, intermediates 5a and 5b were crystallised, and the structures obtained from single crystals grown in methanol are shown in Figure 3(b),(c), respectively. Their X-ray structures are very different, despite the similarity of their compositions. In 5a, the intramolecular hydrogen bonds formed (implicating the methoxy oxygen and the relatively acidic amide proton) facilitates folding of the molecule, which is conducive with complexation. In contrast in 5b, intramolecular hydrogen bonds are less favoured and only intermolecular interactions were identified. This underlies the difference between oxygen and sulphur atoms as hydrogen bond acceptors.

3.2. Photo- and thermal isomerisation

As trans-conformations of azobenzenes in general are thermodynamically more stable than cis-conformations, it is anticipated that at equilibrium in the dark the population of phototartars will consist of 100% trans-form (1-E). Figure 4 shows this to be the case for both 1a (Figure 4(a), solid line) and 1b (Figure 4(b), solid line). This trans-form is characterised by an absorption band around 240 nm attributed to \( \pi \pi^* \) transitions localised on the phenyl groups, a relatively intense band around 360 nm due to symmetry-allowed \( \pi \pi^* \) transitions, which tend to delocalise through the molecule including the two nitrogen atoms, and a weak band around 450 nm originating from symmetry-forbidden \( n \pi^* \) transitions occurring at the central nitrogen atoms (28). On irradiation with UV light (365 nm) the azobenzene unit was successfully isomerised to the cis-form, where the symmetry-allowed \( \pi \pi^* \) transitions band gets weaker and undergoes a hypsochromic shift. The band ascribed to the forbidden \( n \pi^* \) transition also increases slightly (Figure 4(a),(b), dotted line). The photostationary state consists almost exclusively of the cis-form, as judged from changes in the 350-400 nm spectral region, which was verified by NMR (vide infra).

On irradiating the cis-form with visible light (450 nm), the photochemical reversion primarily to the trans-form is effected; however, the photostationary state that is attained after a few minutes of irradiation is not exclusively trans (see Figure 4(a), dashed line). For 1a and 1b, the photostationary state is estimated to consist of 80% and 74% of the trans-form, respectively. The azobenzene can recover completely its original form by thermal isomerisation in the dark, showing that no photodegradation had occurred.

The reversibility of the photoreactions was tested through several irradiation cycles. The insets in Figure 4(a),(b) show the sequential trans-to-cis and cis-to-trans photoisomerisation during six cycles. Each time the same photostationary state is obtained, with only a slight difference between 1a and 1b. Both 1a and 1b are thus photoswitchable and fully reversible over several cycles.

Trans-to-cis photoisomerisations of 1a-E and 1b-E (Figure 5(a),(c)) are almost quantitative according to recorded \(^1\)H NMR spectra, see spectra of photoproducts 1a-Z and 1b-Z (Figure 5(b),(d), respectively), where characteristic signals of trans-forms almost fully disappear. On integrating peak areas, a yield of 94% for 1a and 1b is calculated, which is somewhat higher than related previously reported azobenzenophanes (72%) (11). Quantum yields of trans-to-cis photoisomerisations of 1a (0.66) and 1b (0.65) are three times higher than that of azobenzene (circa 0.2) on irradiating the analogous absorption band (29). This difference may arise from reduced strain on the tether between extremities of the azobenzene on passing to the cis-form from the trans-form (30). Indeed, the mechanism of azobenzene photoisomerisation, which is still a source of contention, may be anticipated to receive contributions from non-sterically demanding in-plane inversion of the angle of the azo-nitrogen atoms or an out-of-plane rotation about the N-N double bond (rotation mechanism) (8, 19, 31-35). Additionally, photoswitching does not affect the chemical shift/chemical environment of the methoxy group.

Thermal cis-to-trans-isomerisations of 1a and 1b were followed spectrophotometrically at 303, 313 and 323 K. The curves tracing the kinetics of changing absorption were fit using Equation (1) (16)

\[
A = (A_0 - A_\infty)e^{\frac{kT}{A_0}} + A_\infty
\]

Here, \( A \) is the measured absorbance, \( A_0 \) is the initial absorbance, \( A_\infty \) is the absorbance when the thermal isomerisation (100% of trans-form) and \( k \) is the rate constant at temperature \( T \). Activation energies (\( E_a \)) were then determined from the Arrhenius equation. Thus, similar \( E_a \) values of 99 and 101 kJ.mol\(^{-1}\) for the thermal cis-to-trans isomerisation of 1a and 1b were noted, respectively. These values are slightly higher than that measured for parent azobenzene measured under identical conditions (90 kJ.mol\(^{-1}\)), pointing to an influence of the macrocyclic tether which may disfavour the rotation mechanism of isomerisation (vide supra).

3.3. Complexation

As the single-crystal X-ray structure showed (Figure 3(a)), 1-E is less geometrically suitable than 1-Z to form ion inclusion complexes. \(^1\)H NMR experiments (see Figure 6) show the formation of metal ligand complexes, in this case with sodium, and offer a means to measure the difference of binding strength between the trans- and cis-forms. Indeed, the singlet resonance at 3.74 ppm, attributed to the
methoxy group protons, is shifted further by Na\(^+\) in the cis-conformation (\(\Delta \delta = 0.47\) ppm cf. \(\Delta \delta = 0.18\) ppm). Equally, some differences in chemical shifts for \(\text{CH}_2\) and aromatic proton resonances can be noted.

Titrations of photolariats with a range of Groups I and II metal cations (as triflate salts), and selected transition metals were performed using \(^1\text{H}\) NMR spectroscopy or spectrophotometry in CD\(_2\)CN or CH\(_3\)CN, respectively. Indeed, the presence of potential axial binders O (1a) or S (1b) is anticipated to affect the stability constants and selectivities of 1a and 1b towards different ions. In \(^1\text{H}\) NMR titrations, several samples with constant concentration of photolariat and variable concentration of cation were analysed. For each signal, the variation in the chemical shift was plotted versus the concentration of cations, for example, Figure 6(e) shows the titration of 1a-
Figure 5. $^1$H NMR spectra of photolariats (2 mM). (a) 1a-$E$, (b) 1a-Z, (c) 1b-$E$, (d) 1b-Z. 1a-$E$ and 1b-$E$ spectra were recorded before any irradiation on samples stored in the dark. 1a-Z and 1b-Z spectra were recorded after irradiation at 365 nm.

Figure 6. Complexation induced changes on $^1$H NMR spectra of photolariat 1a in MeCN (2 mM). (a) 1a-$E$ only, (b) 1a-$E$ with 20 equivalents of sodium triflate, (c) 1a-Z only, (d) 1a-Z with 20 equivalents of sodium triflate, (e) $^1$H NMR chemical shift variation in the CH$_3$O group protons versus number of sodium per ligand. Experimental variations in the chemical shift ($\nu$), fitted curve with calculated values ( ).
Table 1. Photoisomerisation quantum yields, activation energies and binding constants of photolariats 1a and 1b.

<table>
<thead>
<tr>
<th></th>
<th>$^{a} \Phi_0$</th>
<th>$^{b} E_a$ (kJ.mol $^{-1}$)</th>
<th>$^{c} \log K_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a-E</td>
<td>0.66</td>
<td>1.28$^d$, 1.28$^d$</td>
<td>0$^d$, 4.36$^e$</td>
</tr>
<tr>
<td>1a-Z</td>
<td></td>
<td>2.69$^d$, 2.03$^d$, 1.7$^d$</td>
<td>4.41$^e$, 4.67$^e$</td>
</tr>
<tr>
<td>1b-E</td>
<td>0.65</td>
<td></td>
<td>4.78$^e$, 4.81$^e$, 4.62$^e$</td>
</tr>
<tr>
<td>1b-Z</td>
<td>101</td>
<td></td>
<td>4.89$^e$, 4.58$^e$, 3.94$^e$</td>
</tr>
</tbody>
</table>

Notes: (a) Quantum yields of trans-to-cis photoisomerisation ($\Phi_0$ at 365 nm); (b) kinetic constants of thermal cis-to-trans isomerisation; (c) logarithm of binding constants of 1a and 1b with different ions; (d) binding constants determined from $^{1}H$ NMR titrations; (e) binding constants established from spectrophotometric titrations.

Z with sodium (36). Following the spectrophotometric titrations, binding constants were extracted from a Hill plot. All binding constants are shown in Table 1.

Concerning differences of binding affinities between 1a and 1b for transition metal ions tested (Table 1), a slightly higher affinity was observed with S-containing 1b with respect to O-containing 1a. Only, a relatively small difference of binding constant is observed between cis- and trans-forms. This finding can be rationalised if only one of the axial groups (OMe or SMe) and not all of the macrocyclic heteroatoms interact with the bound ion at any given time; thus, the small number of relatively strong interactions is surprisingly similar in the cis- and trans-forms.

4. Conclusion

Incorporation of additional chelating groups in the coordination sphere of azobenzene-containing crown ethers via multi-step syntheses gives photolariats, with photocontrolled binding sites. While the binding constants obtained for a range of different cations finally did not prove superior to previously reported photocrowns, the photochemistry is somewhat different, notably in terms of improved quantum yield, and a photostationary showing quasi-quantitative trans-to-cis conversion. Modifying the macrocyclic linker and axial binders is anticipated to give improved future generations of photolariats. Ultrafast studies of photoinduced isomerisations in photolariats and complexes will be reported in due course.

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References
