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A 'clicked' macrocyclic probe incorporating Binol as the signalling unit for the chiroptical sensing of anions

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ABSTRACT

We describe a macrocyclic chiroptical sensor for the detection of halide anions, with the Binol moiety acting as the CD signalling unit. The macrocycle is conveniently synthesized using CuAAC 'click' reactions in the cyclization step; this methodology installs 1,2,3-triazole moieties within the macrocyclic backbone, able to directionally bind anions by means of CH···X^- hydrogen bonds. ^{1}H NMR complexation studies in $CDCl_3$ reveal weak binding to halide and aliphatic carboxylate anions. Halide anions, however, when held into the macrocyclic cavity, are able to trigger a large chiroptical response originating from the steric interaction with the Binol moiety, which changes its dihedral angle, thus modulating its characteristic CD signature.

1. Introduction

Molecular sensors require the presence of a suitable signalling unit, which usually responds in terms of absorption, emission or electrochemical changes.[1] Circular Dicroism (CD) spectroscopy is extensively used to conveniently monitor conformational changes in complex supramolecular systems, given that CD signals, especially when arising by an exciton-coupled mechanism, can afford information about ligand conformation or absolute configuration that cannot be obtained by other means.[2a] In addition, CD activity can be sensed orthogonally to isotropic absorption signals or to other spectroscopic properties, thus becoming a powerful tool for sensing, especially when the response obtained from isotropic techniques are particularly weak. It has been possible to devise receptors—i.e., chiroptical sensors—able to detect the binding of a target analyte by responding with a variation of the CD activity resulting from the formation of a sensor molecule/analyte ensemble.[2b] Several examples of chiroptical sensors that provide significantly differentiated CD signals upon binding of a metal ion,[3] of neutral guests,[4] or chiral polymers[5] have been recently reported.

Shape-persistent macrocycles obtained by the CuAAC (Copper Catalyzed Azide–Alkyne Cycloaddition) reaction have recently emerged as outstanding candidates for recognition and sensing of anions in organic solutions. The 'click' reaction is not only useful and high-yielding in the macrocyclization step, but it is also efficient in installing triazole functionalities, in which the acidic CH protons act as efficient hydrogen-bonding donors in the complexation of anions, detected using NMR, UV/vis or fluorescence spectroscopies.[6] Binol-based synthons are a robust source of chirality; they are widely used in asymmetric catalysis, and applications in the fields of sensing and materials science are being increasingly developed.[7,8]

We and others have reported how conformational changes, brought about by variations in the macrocyclic skeletons[9a] or by substituents with differing steric demand,[9b] induce an alteration of the dihedral angle between the naphthyl planes of the binaphthyl unit. This alteration can be efficiently signalled by large variations in the intensity of the exciton-coupled CD signal, the classical signature of resolved binaphthyl units. These units can therefore be envisaged as good CD reporters in the design of chiroptical sensors.

In this paper, we describe the design, synthesis and characterization of a chiroptical macrocyclic sensing molecule, with embedded anion-recognizing 'handles', in the form of the CH functionalities of 1,2,3-triazole units. These moieties hold the anion in proximity of the neighbouring binaphthyl moiety, which is the signalling unit (Fig. 1).

2. Results and discussion

2.1. Synthesis

The synthesis of the 'tweezer-like' model compound (*R*)-**6** and of macrocycle (*R*)-**7** is reported in Scheme 1. Preliminary molecular

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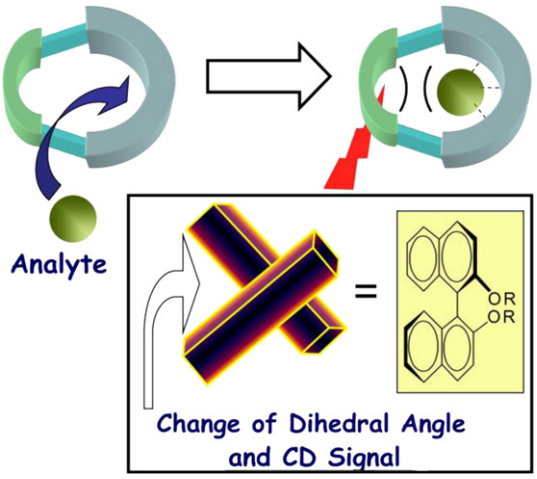
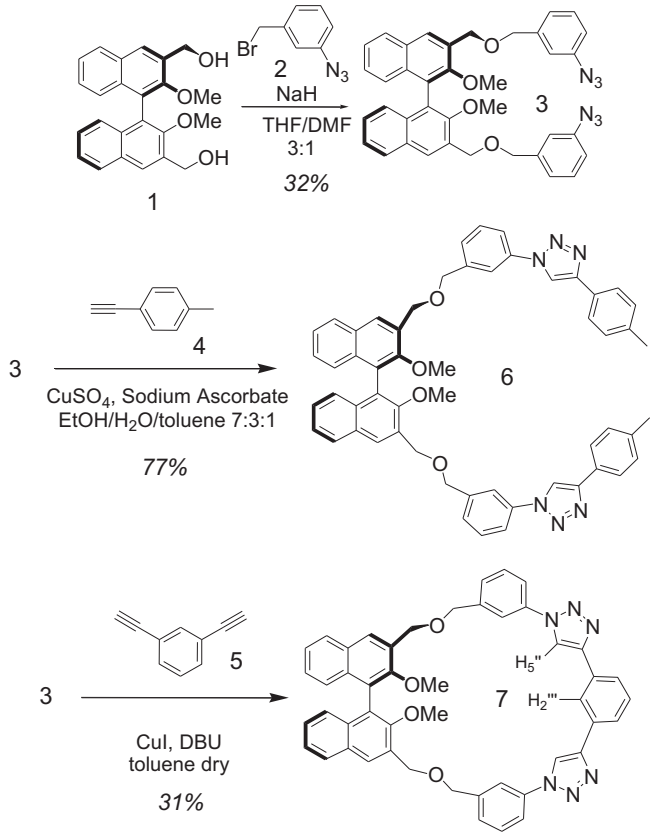


Fig. 1. General design of a macrocyclic chiroptical sensor in which the variation of the CD response of the Binol unit is the key sensing output.



Scheme 1. Synthesis of the open analogue (*R*)-**6** and the clicked macrocycle (*R*)-**7**.

modelling, along with experimental results from our group, suggested that, in order to counterbalance the inherent distortion brought about by the insertion of the binaphthyl unit into the macrocyclic framework (Fig. 1), some elements of conformational flexibility, such as sp^3 carbon atoms, imparting a higher conformational freedom with respect to sp or sp^2 hybridized carbon atoms, needed to be introduced. Elaboration of the optically-pure benzylic diol (*R*)-**1** (Scheme 1) was carried out by means of Williamson ether synthesis with aromatic azide-containing benzyl bromide **2**, to generate advanced intermediate (*R*)-**3** in good yields. For the synthesis of model compound (*R*)-**6**, in which the two triazoles are not embedded into a rigid macrocyclic skeleton, yet they are free to rotate and rearrange, we used classical CuAAC conditions[10] with precursors (*R*)-**3** and commercially-available aromatic terminal alkyne **4**, which produced compound (*R*)-**6** in good yields. Conversely, when the classical CuAAC conditions were applied to the synthesis of macrocycle (*R*)-**7**, even in high dilution conditions, we could not isolate cyclic material, but rather the formation of polymeric baseline material was observed.

We therefore used previously reported conditions for CuAAC macrocyclizations,[11] in which the terminal alkyne fragment is added to a solution of base and Cu(I) catalyst, rather than generating the Cu(I) catalytic species in situ. By this procedure, the macrocycle could be isolated in satisfactory yields (31%) after chromatography, and fully characterized by NMR spectroscopy and mass spectrometry. Compound (*R*)-**6** and macrocycle (*R*)-**7** showed the major absorption band centred around 230 nm, typical of the binaphthyl chromophore, with molar absorption coefficient values (ε=70.000–150.000 M^{-1} cm^{-1}) within the range of those already reported for this class of absorbers.[8] Other bands, with maxima in the 250–300 nm range (Fig. S1), are consistent with compounds containing equivalent conjugated fragments.[11] CD spectroscopy of compounds (*R*)-**3**, (*R*)-**6** and (*R*)-**7** showed the exciton-coupled structure typical of binaphthyl moieties (Fig. S2), corresponding to the maximum absorption band in the UV/vis spectra. No induced CD activity could be associated with other chromophores and absorption bands in the UV/vis spectra.

Macrocycle (*R*)-**7**, furthermore, did not show any deviation from linearity in its Lambert–Beer behaviour over a wide range of concentrations, both in CH_2Cl_2 and in nonpolar solvents, such as *n*-hexane. In shape-persistent macrocycles, sterically-hindering *tert*-butyl groups are frequently introduced within the framework, to improve solubility and to prevent aggregation.[12] The absence of such functionalities in the case of macrocycle **7** could lead to potential aggregation behaviour by stacking of the extended aromatic hemicyclic bay of macrocycle **7**, which is however not observed.

2.2. Complexation studies

^{1}H NMR titration experiments in $CDCl_3$ showed binding of a series of anions (Table 1) to both open analogue (*R*)-**6** and macrocycle (*R*)-**7**. Maximum complexation-induced shifts (Table S1) were generally low, but well above the experimental limit of the instrument and of the analysis method.[13] The corresponding association constants could be obtained by fitting the data to a 1:1 binding model.

An ascending trend in terms of overall affinity (Table 1) in the halide series could be observed, going from fluoride to iodide for both the macrocycle (*R*)-**7** and the open system (*R*)-**6**. Anion binding by neutral receptors in $CDCl_3$ is often very weak as the receptor has to compete against ion pairing; however, neat $CDCl_3$ was in our case the most suitable solvent given the excellent

Table 1
Binding constants (M^{-1}) for the 1:1 complexes between 'open analogue' (*R*)-**6** and macrocycle (*R*)-**7** and anions in $CDCl_3$[a]

Anion	Compound **6**	Macrocycle **7**
F^-	[b]	[b]
Cl^-	7.4±0.3	8.9±0.0
Br^-	10.6±0.4	12.5±1.8
I^-	11.4±0.5	18.1±3.2
CH_3COO^-	[b]	15.5±2.3
(*S*)-Mandelate	[b]	14.3±1.2
(*R*)-Mandelate	[b]	8.6±0.7

[a] Measured by ^{1}H NMR (500 MHz, 298 K, $CDCl_3$) using tetrabutylammonium salts.
[b] No quantifiable binding was detected.

solubility of the hosts and the tetrabutylammonium salts used. We also tested carboxylate anions, and again weak association constants characterized the binding events in $CDCl_3$; by utilizing chiral guests (mandelate anions) a moderate degree of enantiodiscrimination was observed in the case of macrocycle (*R*)-**7**.

The similar behaviour shown by the closed and open compounds indicates that size match and preorganization—which determine a 'best fit' in correspondence to a certain halide anion in the case of previously reported shape-persistent macrocycles—is not a key issue in the case of compound (*R*)-**7**.[11] Inspection of the ^{1}H NMR titrations revealed that the major shift upon complexation is that observed for the triazole CH hydrogen atoms of the hosts, indicating that the mode of complexation mainly involves, as expected, these functional groups (Fig. 2).

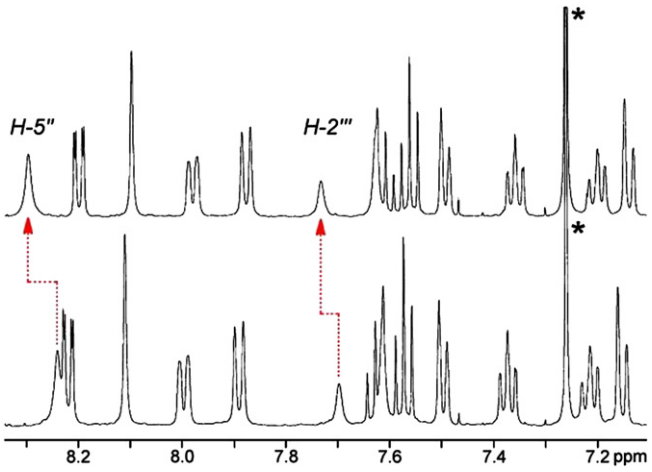


Fig. 2. Aromatic region of the ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C) spectra of macrocycle (*R*)-**7** (2.5 mM, bottom) and at the end of the titration with Bu_4NI ([(*R*)-**7**]=2.5 mM, [Bu_4NI]=50 mM, top).

Geometry optimization carried out at the semi-empirical (PM3) level (Figs. S3–S5) on the 1:1 complexes shed light on the binding mode of anions to the open compound (*R*)-**6** and to macrocycle (*R*)-**7**. In all the cases examined, complexation is driven by the affinity of the anions to the triazole CH hydrogen atoms. In particular, the carboxylate anions bind in a bridge-like fashion with the two oxygen atoms pointing towards the two triazole CH groups. In the case of macrocycle (*R*)-**7**, spherical (i.e., halide) anions dock in the cleft generated by the triazole units and the *m*-phenylene spacer,[6] enjoying an additional interaction with a CH hydrogen atom of the latter aromatic unit, as confirmed by the complexation-induced shifts observed during the ^{1}H NMR titrations. On binding halide anions, the peak belonging to H-2‴ (the CH hydrogen atom of the *m*-phenylene spacer placed between the triazole units, Scheme 1) undergoes complexation-induced shifts about three times larger than those observed upon carboxylate binding. In addition, molecular modelling clearly indicated, in macrocycle (*R*)-**7**/halide complexes, that the spherical anions sterically interact with the Binol unit modifying its dihedral angle.

2.3. CD spectroscopy

The intensity of the low energy branch of the exciton-coupled CD signal associated with the Binol moiety can be directly related to the dihedral angle of the binaphthyl unit.[9] It should be stressed that even large variations in the maximum value of the low energy component of the couplet correspond to little changes in the dihedral binaphthyl angle.

The inherent UV absorbance of CH_2Cl_2 or other chlorinated solvents made the use of the 210–230 nm spectral range not practical in UV/vis or CD spectroscopies at the low concentrations (10^{-5}–10^{-6} M) required by the relatively high molar extinction coefficient values of our Binol-containing receptors in this spectral region. Seeking to develop the Binol moiety as the CD signalling unit, we changed the solvent mixture in order to obtain a tradeoff between solubility of the anions (used as their tetrabutylammonium salts), and optical transparency in the 210–230 nm spectral range.

Indeed, when titrating macrocycle (*R*)-**7** with Bu_4NI in a methylcyclohexane (MCH)/CH_2Cl_2 (9/1) solvent mixture, a large variation of the CD signal could be observed (Fig. 3). Similar titration profiles could be observed in the presence of halide anions of differing steric hindrance, such as Br^- and Cl^-, but the effect was not observed in the presence of fluoride (Fig. 4). This effect was also not observed in the case of all carboxylate anions tested. For all CD-active halides (I^-, Br^- and Cl^-), the CD intensity initially decreased up to a maximum value and then slightly increased when the guest concentration exceeded a certain point (after 6–10 equiv guest, see inset), suggesting that a competition of bridging versus nonbridging complexations might be in place under excess guest conditions.[14]

The open analogue (*R*)-**6**, for which complexation with halide anions has been substantiated by ^{1}H NMR spectroscopy, did not show any CD response, probably as a result of the innate conformational freedom enjoyed by the open structure, which allows for a minimization of the steric interaction of the anions with the binaphthyl unit. Control experiments with Binol precursor (*R*)-**1** excluded any alternative binding mechanism (e.g., anion–π interactions) as the source of the CD output in the investigated solvent system (Fig. 4).[15] Even more interestingly, the sensing macrocyclic molecule is silent upon titration with halide or carboxylate anions using UV/vis detection (Fig. S9).

3. Conclusions

We have presented the synthesis and characterization of a novel macrocycle as a chiroptical sensor for halide anions. The signalling mechanism is substantially different from previously reported examples of chiroptical sensor for anions;[6b,c] in fact, it is not a result of a specific recognition of the analyte with the CD reporter, the Binol moiety, but rather a secondary effect. The active anions are held into the cavity by specific hydrogen-bonding interactions with triazole CH moieties; they are in close proximity of the Binol moiety, and its conformational change generates strong signalling *exclusively* when CD spectroscopy is used as the detection tool. The system shows selectivity towards iodide, bromide and chloride over fluoride and carboxylate anions.

This report highlights the potential of CD spectroscopy as a signalling technique that can be used, with suitably designed molecular receptor systems, orthogonally and in a complementary way to other more direct, isotropic sensing techniques, such as absorbance or emission spectroscopies. We are currently aiming at more refined, highly specific molecular chiroptical sensors for the detection of suitable substrates within complex analyte matrices, especially useful when other, more widely used analytical techniques suffer interference from competing substrates in the matrices.

4. Experimental section

4.1. General

All commercially-available reagents and solvents were used as received. THF (Na, benzophenone) and CH_2Cl_2 (CaH_2) were dried and distilled before use. CCl_4 (for the NBS bromination) and toluene

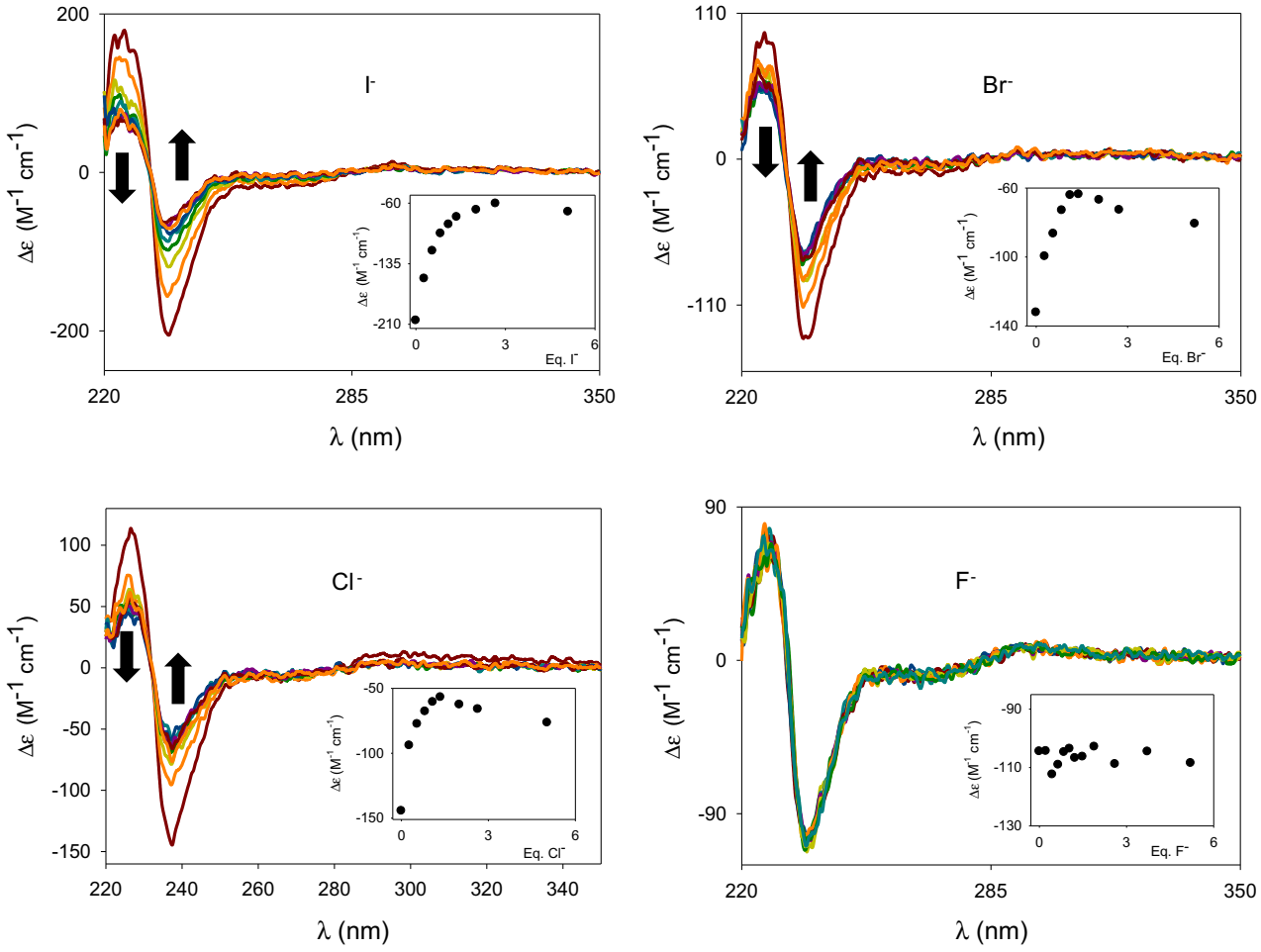


Fig. 3. CD titrations of macrocycle (*R*)-**7** with increasing amounts of Bu_4NX in MCH/CH_2Cl_2 9:1 (v/v). Fixed host concentration: 5.2×10^{-6} M; guest concentration: see inset (for inset, values at 235 nm, for the lowest energy branch of the CD couplet, are plotted vs added guest equivalents).

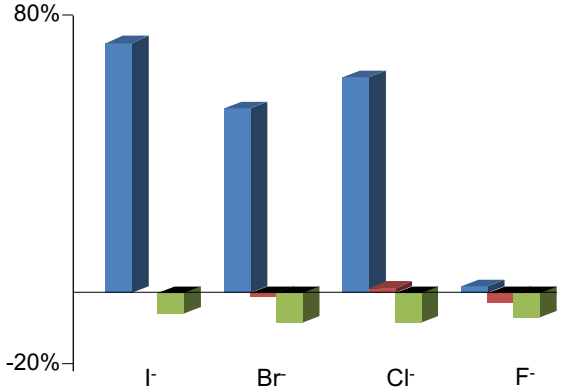


Fig. 4. Reduction (%) of the lower energy branch of the exciton-coupled CD signal of the binaphthyl moiety for macrocycle (*R*)-**7** (blue), compound (*R*)-**6** (green) and control (*R*)-**1** (red) upon complexation with halide anions in MCH/CH_2Cl_2 9:1 (v/v) (see Fig. 3 and S7–S8).

were dried using 4 Å molecular sieves. Compound (*R*)-**1**[16] was obtained following previously published procedures. Compound **2**[17] was obtained through: (a) diazotization reaction and azide formation starting from 3-methylaniline;[18] (b) NBS bromination.[17] Analytical thin layer chromatography was performed on silica gel, chromophore loaded, commercially-available plates. Flash chromatography was carried out using silica gel (pore size 60 Å, 230–400 mesh). ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on 200, 300 or 500 MHz spectrometers using the residual solvent peak or tetramethylsilane as the standard. The UV/vis spectroscopic studies were recorded using commercially-available spectrophotometers. Mass spectra were recorded using an electrospray ionization instrument. Optical rotations were measured on a polarimeter with a sodium lamp (λ=589 nm) and are reported as follows: $[\alpha]_D^{rt}$ (c=g (100 mL)$^{-1}$, solvent). CD spectroscopy was performed using a spectropolarimeter; spectra were recorded at 25 °C at a scanning speed of 20 nm min^{-1} and were background corrected.

4.2. ^{1}H NMR complexation experiments

All spectra were recorded at 500 MHz and at 298 K. K_a values for the complexation of (*R*)-**6** or (*R*)-**7** with *n*-$Bu_4N^+X^-$ (X^-=F^-, Cl^-, Br^-, I^-, AcO^-, (*S*)-(+)-PhCH(OH)CO_2^-, (*R*)-(−)-PhCH(OH)CO_2^-) were assessed by nonlinear treatment of the data obtained from ^{1}H NMR titration experiments. Samples were prepared by adding to a 0.5 mL solution of the host (5 mM in $CDCl_3$) successive aliquots of a stock solution of the guest (62.5 mM in $CDCl_3$) to a final volume of 1.0 mL. Eight values of δ_{obs} for the triazole CH resonances were collected by keeping the [host] to [guest] ratio in the 1/0.25–1/12.5 interval. Nonlinear regression analysis of δ_{obs} versus [guest], using the WinEQNMR for Windows software package,[19] provided the K_a value.

4.3. General procedure for the UV/vis or CD titration experiments

Methylcyclohexane (MCH) was purchased as UV/vis spectroscopic grade and used as received. An analytical balance (with a precision of 10^{-4} g) was used to weight the samples for the stock solutions. Aliquots of these stock solutions were then taken via high precision syringes to prepare the cuvette samples for spectrophotometric analyses. *Titration experiments*. The titration experiments were conducted as follows: to a stock solution of the host (solution A) in CH_2Cl_2 or MCH/CH_2Cl_2, several aliquots of the guest (the tetrabutylammonium salt, solution B) were added. Solution B is formed by the tetrabutylammonium salt at higher concentration dissolved in solution A, in order to maintain the host always at a constant concentration.

4.4. Molecular modelling

The conformational analysis of (*R*)-**6** or (*R*)-**7** and their complexes were carried out with the classical molecular mechanics force field (MMFF) by using the Monte Carlo method to randomly sample the conformational space. The equilibrium geometry obtained for the minimum-energy conformer (*R*)-**6** or (*R*)-**7** was refined at the PM3 semi-empirical level. The equilibrium geometry of the complexes were calculated using the molecular mechanics force field from the optimized geometry of the receptor, by placing the anion(s) at a short distance from the triazole CH hydrogen atoms and leaving the system free to relax without constraints. The conformer obtained was further refined by semi-empirical methods at the PM3 level. All calculations were performed using Spartan'10 (Wavefunction, Inc., Irvine, CA).[20]

4.5. Synthesis of compounds

*4.5.1. Compound (R)-**3**.* Compound (*R*)-**1** (0.303 g, 0.81 mmol, 1 equiv) was added to a solution of NaH (0.088 g, 3.64 mmol, 4.5 equiv) in THF/DMF 3:1 (20 mL). A solution of **2** (0.429 g, 2.02 mmol, 2.5 equiv) in THF (3 mL) was then added. The suspension was stirred overnight and H_2O (5 mL) was added. The THF was removed in vacuo, then the mixed aqueous layer was extracted with CH_2Cl_2 (3×15 mL). The crude product was purified by flash chromatography (SiO_2; hexanes/AcOEt: 95/5 to 8/2) to afford **3** (164 mg, 32%) as a white solid; [found: C 71.5, H 5.0. $C_{38}H_{32}N_6O_4$ requires C 71.7, H 5.1%]; $[\alpha]_D^{25}$ −25.9 (*c* 0.007, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz, 25 °C) δ=8.13 (s, 2H; *H*4 binaphthyl), 7.94 (d, 2H; *J*=8.1 Hz, binaphthyl), 7.45–7.18 (m, 12H; binaphthyl+Ar–*H*), 7.21 (m, 4H; binaphthyl), 7.01 (d, 2H; *J*=7.8 Hz, Ar–*H*), 4.91 (AB system, 4H; *J*=12.4 Hz, C*H*$_2$), 4.76 (s, 4H; C*H*$_2$), 3.30 (s, 6H; –OC*H*$_3$). ^{13}C NMR ($CDCl_3$, 75 MHz, 25 °C) δ=154.6 (C_q), 140.4 (C_q), 140.2 (C_q), 133.9 (C_q), 131.4 (C_q), 130.4 (C_q), 129.7 (CH), 128.9 (CH), 128.0 (CH), 126.3 (CH), 125.6 (CH), 124.8 (CH), 124.3 (C_q), 124.1 (CH), 118.2 (CH), 118.1 (CH), 72.2 (CH_2), 68.2 (CH_2), 61.0 (OCH_3). MS (ESI) *m*/*z* (%): 659 ([M+Na]$^+$, 100), 1294 ([2M+Na]$^+$, 6).

*4.5.2. Compound (R)-**6**.* Compound (*R*)-**3** (34 mg, 0.053 mmol, 1 equiv) was added to a solution of 4-ethynyltoluene **4** (0.014 mL, 0.106 mmol, 2 equiv), sodium L-(+)-ascorbate (2 mg, 0.0106 mmol, 0.2 equiv) and $CuSO_4$ (1 mg, 0.0053 mmol, 0.1 equiv) in EtOH/H_2O/toluene 7:3:1 (1.1 mL). The homogeneous solution was stirred for 48 h at room temperature. The solution was partitioned into two layers by adding CH_2Cl_2, and the aqueous layer was extracted with clean CH_2Cl_2 (3×5 mL). The combined organic layers were dried (Na_2SO_4), and the product was purified by flash chromatography (SiO_2; hexanes/AcOEt: 9/1 to 7/3) to afford (*R*)-**6** (31 mg, 77%) as a white solid [found C 77.5, H 5.3. $C_{56}H_{48}N_6O_4$ requires C 77.4, H 5.6%]; $[\alpha]_D^{25}$ −18.1 (*c* 0.005 in CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C) δ=8.17 (s, 2H; H5″), 8.11 (s, 2H; H4), 7.92 (dt, 2H; *J*=8.1, 0.7 Hz, H8), 7.62 (m, 2H; H2′), 7.78 (d, 4H; *J*=8.0 Hz, H2‴), 7.74 (ddd, 2H; *J*=7.6, 2.2, 1.4 Hz, H6′), 7.53 (part of an ABX system, 2H; J_{AB}=7.6 Hz, J_{AX}=7.6 Hz, H5′), 7.50 (part of an ABX_2 system, 2H; J_{AB}=7.6 Hz, J_{AX}=1.4 Hz, H4′), 7.40 (ddd, 2H; *J*=8.1, 6.9, 1.5 Hz, H7), 7.26 (d, 4H; *J*=8.0 Hz, H3‴), 7.20–7.25 (m, 2H, H6), 7.16–7.19 (m, 2H, H5), 4.94 and 4.88 (AB system, 4H; J_{AB}=12.4 Hz, Binol–CH_2), 4.82 (s, 4H; benzylic–CH_2), 3.28 (s, 6H; OCH_3), 2.40 (s, 6H; CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 25 °C) δ=154.7, 140.6, 138.3, 137.3, 134.0, 131.3, 130.5, 129.8 (C5′), 129.6 (C3‴), 129.2 (C4), 128.1 (C8), 127.8 (C4′), 127.4 (C_q), 126.5 (C6), 125.7 (C2″), 125.6 (C5), 125.0 (C7), 124.4 (C_q), 119.7 (C6′), 119.6 (C2′), 117.3 (C5″), 72.0 (Binol–CH_2), 68.4 (benzylic–CH_2), 61.1 (OCH_3), 21.3 (CH_3). MS (ESI) *m*/*z* (%): 891 ([M+Na]$^+$, 23), 869.0 ([M+H]$^+$, 100).

*4.5.3. Macrocycle (R)-**7**.* 1,8-Diazabicyclo[5.4.0]undec-7-ene (742 mg, 4.88 mmol, 20 equiv) was dissolved in dry toluene (100 mL) and N_2 was bubbled through the solution for 15 min. The solution was heated at 70 °C for 30 min and CuI (23 mg, 0.122 mmol, 0.5 equiv) was added as a solid. A solution of compound (*R*)-**3** (155 mg, 0.244 mmol, 1 equiv) and 1,3-diethynylbenzene **5** (31 mg, 0.244 mmol, 1 equiv) in dry toluene (40 mL) was added dropwise over a period of 10 h while keeping the reaction mixture under inert atmosphere. The reaction was stirred at room temperature for 4 h. H_2O (100 mL) was added and the reaction mixture extracted with CH_2Cl_2 (3×100 mL). The product was purified by flash chromatography (SiO_2; hexanes/AcOEt: 9/1 to 7/3) to afford (*R*)-**6** (58 mg, 31%) as a white solid [found C 75.5, H 5.3. $C_{48}H_{38}N_6O_4$ requires C 75.6, H 5.0%]; $[\alpha]_D^{25}$ −11.6 (*c* 0.001 in CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C) δ=8.28 (s, 2H; H5″), 8.21 (dd, 2H; *J*=7.6, 1.3 Hz, H4‴), 8.11 (s, 2H; H4), 7.97 (ddd, 2H; *J*=7.9, 2.0, 1.1 Hz, H4′), 7.89 (dd, 2H; *J*=8.1, 1.3 Hz, H8), 7.71 (br s, 1H; H2‴), 7.62 (br s, 2H; H2′), 7.59 (t, 1H; *J*=7.6 Hz, H5‴), 7.56 (t, 2H; *J*=7.9 Hz, H5′), 7.50 (dt, 2H; *J*=7.9, 1.1 Hz, H6′), 7.37 (ddd, 2H; *J*=8.1, 6.7, 1.3 Hz, H7), 7.21 (ddd, 2H; *J*=8.6, 6.7, 1.3 Hz, H6), 7.15 (dd, 2H; *J*=8.6, 1.3 Hz, H5), 4.96 and 4.87 (AB system, 4H; *J*=11.6 Hz, benzylic–CH_2), 4.85 and 4.79 (AB system, 4H; *J*=12.1 Hz, Binol–CH_2), 3.27 (s, 6H; CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 25 °C) δ=154.8, 147.8, 140.1, 137.1, 134.0, 131.1, 2× 130.5, 130.2 (2C, C4), 130.1 (3C, C5′ and C5‴), 130.0, 128.6 (C6′), 128.1 (C8), 126.6 (C6), 126.2 (C4‴), 125.6 (C5), 125.1 (C7), 124.5, 123.3 (C2‴), 121.0 (CH-4′), 119.7 (C2′), (C6′), 118.3 (C5″), 72.6 (Binol–CH_2), 68.8 (benzylic–CH_2), 61.4 (OCH_3). MS (ESI) *m*/*z* (%): 785.3 ([M+Na]$^+$, 100), 1548.1 ([2M+Na]$^+$, 28).

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Supplementary data

Supplementary data contain additional NMR, UV and CD spectra, titrations and computational details associated with this article. Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2012.07.038.

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