Synthesis of α-cyclodextrin [2]-rotaxanes using chlorotriazine capping reagents

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Ten α-cyclodextrin [2]-rotaxanes have been prepared with alkane-, stilbene- and azobenzene-based axles, capped through nucleophilic substitution of either 2-chloro-4,6-dimethoxy-1,3,5-triazine or 2,4-dichloro-6-methoxy-1,3,5-triazine in aqueous solution, followed by further substitution of the remaining triazinyl chlorine in some cases when the latter capping reagent was used. In one case the rotaxane is a [c_2]-daisy chain obtained by double-capping the corresponding hermaphroditic cyclic dimer. One of the rotaxane azobenzene derivatives was shown to undergo photochemically-induced reversible interconversion between its *trans*- and *cis*-isomers, causing the cyclodextrin to move back and forth along the axle, and therefore behave as a molecular shuttle. The methodology is therefore shown to constitute a general and versatile approach for the construction of supramolecular species as the basis of photochemical molecular devices.

Introduction

[2]-Rotaxanes are suitable building blocks for the assembly of supramolecular species, each consisting of a macrocycle threaded on an axle that is capped or blocked with bulky end groups to prevent the dissociation of the components.[1] They are of interest as building blocks for the construction of nanotechnological devices. Cyclodextrins (CDs) are well-suited as the macrocycles for rotaxane synthesis.[2–6] The structures of α- and β-CD are shown in Fig. 1. Their hydrophobic interiors and hydrophilic exteriors promote the formation of inclusion complexes with hydrophobic guests in aqueous solution. Capping each end of an encapsulated guest then produces a [2]-rotaxane *via* what is termed the threading method.[7,8]

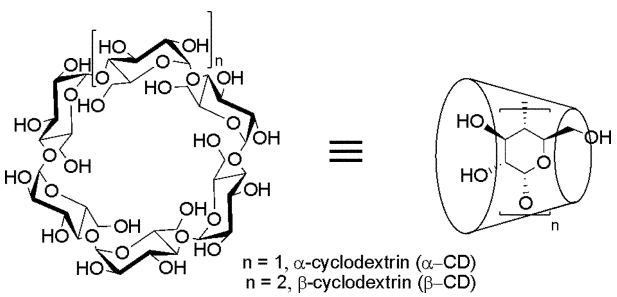

Fig. 1 Structures of α- and β-cyclodextrin (left) and their schematic representation as a truncated cone (right).

A variety of reactions have been utilised in the construction of CD-based [2]-rotaxanes. These include metal coordination,[9–12] Suzuki coupling,[13–20] amide coupling,[21–24] alkylation[25,26] and nucleophilic aromatic substitution.[27–36] The last of these has most often been accomplished using 2,4,6-trinitrobenzenesulfonic acid as the capping reagent,[27–34] but the product rotaxanes are either photochemically inert or unstable, which severely compromises their utility as molecular devices. Here we report a range of examples of the use of 2-chloro-4,6-dimethoxy-1,3,5-triazine (**7**) and 2,4-dichloro-6-methoxy-1,3,5-triazine (**13**) as complementary capping reagents for α-CD-based rotaxane synthesis, also through nucleophilic substitution.

At the outset of this study, Kunitake *et al.*,[37] had already used the bulky dichlorotriazine **2** to prepare the β-CD rotaxane **3**, which through reaction with aniline **4** afforded the derivative **5** (Scheme 1). The Anderson group[38] had also employed 2,4,6-trichloro-1,3,5-triazine to prepare a hexakis(2,3,6-tri-*O*-methyl)-α-CD rotaxane, which had been further elaborated through sequential displacement of the remaining triazinyl chlorines. However, other chlorotriazines had not been studied, and it was not clear if the chlorotriazines **7** and **13** would be effective blocking reagents, reacting selectively with guests complexed by α-CD rather than either the corresponding free guests, the nucleophilic hydroxy groups of the CD or the water required to induce guest complexation, particularly under the basic conditions necessary to maintain the nucleophilic reactivity of the guest. The Anderson group explained that they chose to use the termethylated α-CD in order to prevent coupling between the trichlorotriazine and the CD.

Results and discussion

In the event such processes did not complicate the synthesis of rotaxanes using unmodified α-CD. In a typical procedure, illustrated in Scheme 2, a solution of α-CD and the diamine **6** in 0.2 M carbonate buffer at pH 10 was stirred at room temperature for 2 h, to allow inclusion complex formation, before the chlorotriazine **7** was added and the mixture was stirred for a further 12 h. Product formation was monitored by TLC, which showed a component with an R_f value higher than that of α-CD,

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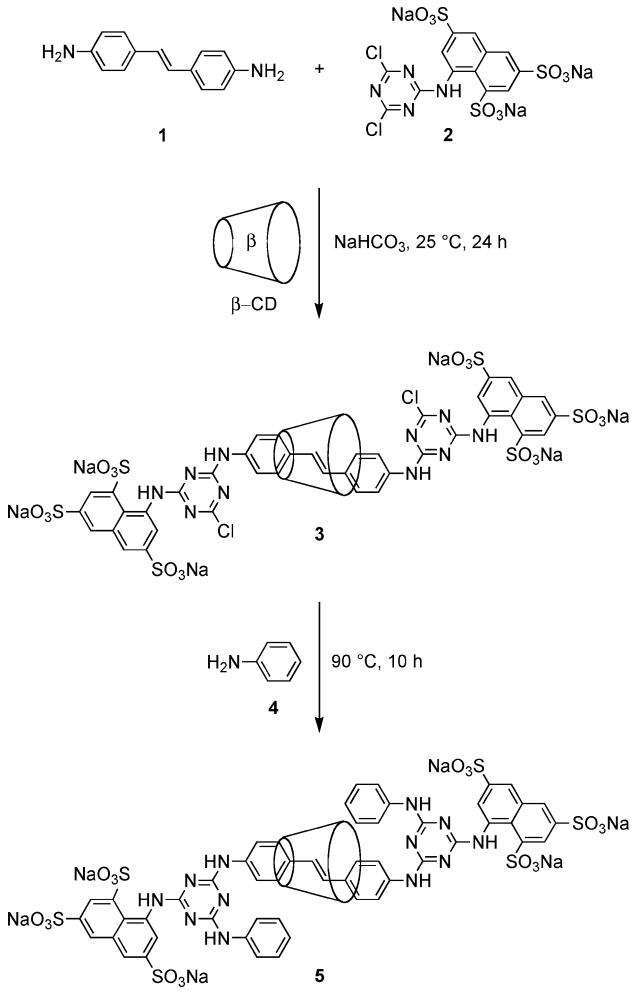
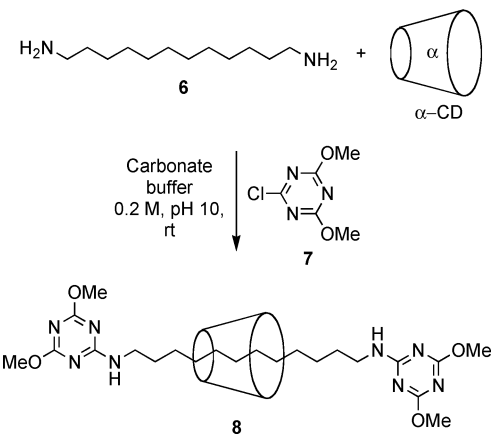


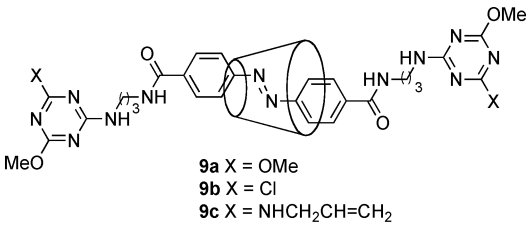
Scheme 1 Formation of the triazine-capped β-cyclodextrin [2]-rotaxanes **3** and **5** as reported by Kunitake *et al.*[37]

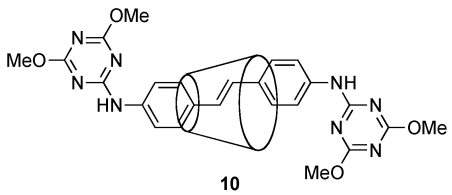


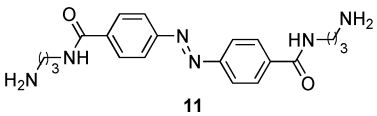
Scheme 2 Synthesis of the rotaxane **8**.

and having both the UV absorbance of an aromatic compound and the characteristic pink colouration of a CD on exposure to acidic naphthalene-1,3-diol.[28,29] This material was isolated by chromatography on a Diaion HP-20 column and identified as the rotaxane **8**, which was obtained in 25% yield.

In a similar manner, the rotaxanes **9a** and **10** were prepared in yields of 31% and 5%, respectively, using the azobenzene **11** and the diaminostilbene **1** instead of the diamine **6**. In the latter case, triethylamine was used as an alternative to carbonate to control the pH of the reaction mixture, and the product was isolated using HPLC.



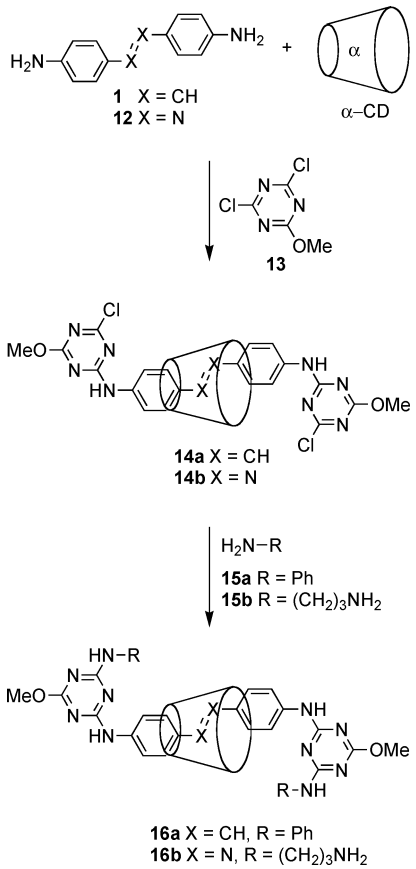




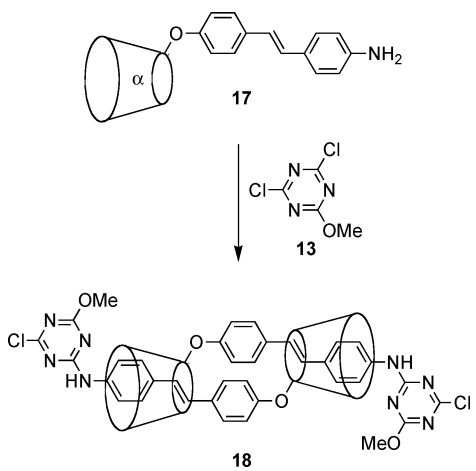
The dichlorotriazine **13** is understood to be generally more reactive and less selective towards nucleophilic substitution than the monochloride **7**.[39,40] Nevertheless, it reacted with the diaminostilbene **1** and the diaminoazobenzene **12** in the presence of α-CD, under conditions analogous to those described above, to give the rotaxanes **14a** and **14b**, in yields of 20% and 19%, respectively (Scheme 3). The labile chlorines of the rotaxanes **14a** and **14b** provide versatility for further functionalisation, as exemplified in the earlier reports of Kunitake *et al.*,[37] and the Anderson group.[38] Accordingly, reactions with aniline **15a** and 1,3-diaminopropane **15b** gave the rotaxanes **16a** and **16b**, in yields of 33% and 76%, respectively. Under closely related conditions, the diamine **11** reacted with the dichlorotriazine **13** in the presence of α-CD to give a 5% yield of the rotaxane **9b**, which reacted with allylamine to give the rotaxane **9c** in 59% yield.

As the final example of a methoxytriazine-capped rotaxane, treatment of the hermaphroditic[29,41] stilbenyl-α-CD **17**[42] with the dichlorotriazine **13** afforded the [*c*2]-daisy chain **18** in 13% yield (Scheme 4). The dimeric nature of this species was established using mass spectrometry and the symmetry inherent in the cyclic structure, as distinct from the corresponding linear daisy chain, was apparent from the simplicity of the 1D ^{1}H NMR spectrum.

The rotaxanes **8**, **9a–c**, **10**, **14a**,**b**, **16a**,**b** and **18** were fully characterised. In each case, ^{13}C and 1D ^{1}H NMR spectroscopy were used to confirm the identity of the macrocyclic and axle components, which were shown by TLC, HPLC and mass spectrometry to be physically interlocked as a supramolecular entity and unable to dissociate. The preferred conformations of the rotaxanes in MeOH-d_4 and DMSO-d_6 were determined using DQCOSY and ROESY ^{1}H NMR spectroscopy. With the rotaxanes **9a–c**, **10**, **14a**,**b**, **16a**,**b** and **18**, NOE interactions in the ROESY spectra show



Scheme 3 Synthesis of the rotaxanes **14a**,**b** and **16a**,**b**.



Scheme 4 Synthesis of the rotaxane **18**.

that the CD is located over the azobenzene or stilbene moiety, as illustrated in Fig. 2 and 3 for the rotaxanes **9a** and **14a**, respectively.

One of the objectives of the current work was to establish chemistry to underpin the development of photochemical molecular devices. As a preliminary assessment of the utility of methoxytriazine-capped rotaxanes in this area, the photochemical behaviour of the azobenzene derivative **9a** was examined. Generally, stilbenes and azobenzenes can undergo reversible interconversion between their *trans*- and *cis*-isomers upon irradiation, and the direction is determined by the wavelength of incident

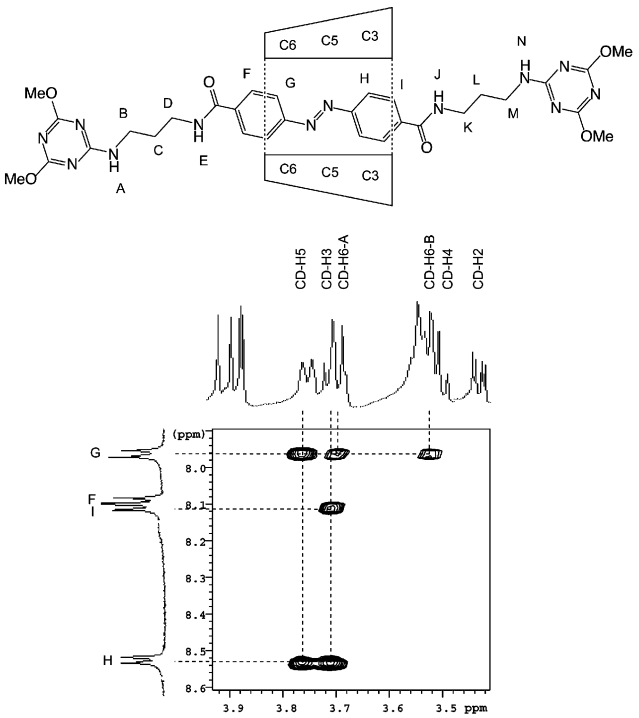


Fig. 2 A section of the 500 MHz 2D ROESY NMR spectrum of the [2]-rotaxane **9a** in MeOH-d_4 at 25 °C, showing crosspeaks between azobenzene and cyclodextrin proton signals.

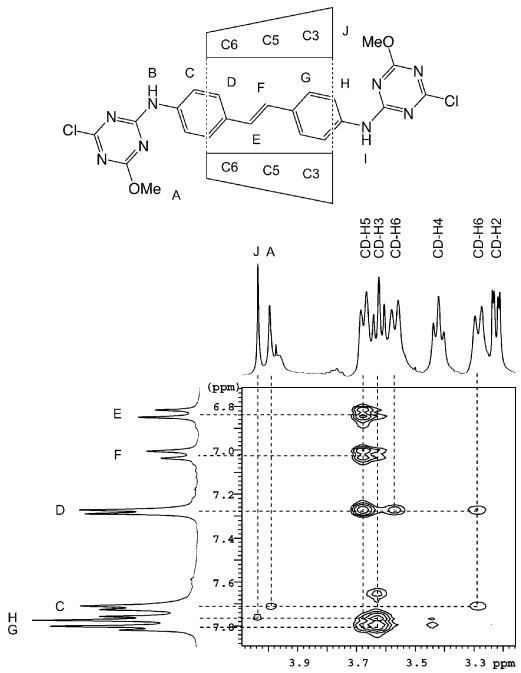


Fig. 3 A section of the 500 MHz 2D ROESY NMR spectrum of the [2]-rotaxane **14a** in DMSO-d_6 at 25 °C, showing crosspeaks between stilbene and cyclodextrin proton signals.

light.[43–46] This has been exploited in the development of CD-based molecular shuttles.[15,35,36]

Irradiation at 350 nm of a dilute aqueous solution of the rotaxane **9a** afforded a 60 : 40 mixture of the starting material and the *cis*-isomer **19**, at the photostationary state, as determined using

HPLC and UV–visible spectroscopy. When solutions containing the *cis*-rotaxane **19** were irradiated at 420 nm or left standing under normal laboratory lighting, complete conversion back to the *trans*-isomer **9a** was observed. A sample enriched in the *cis*-rotaxane **19** was isolated through HPLC. Its ROESY spectrum recorded in MeOH-d_4 shows no NOE interactions between CD and azobenzene protons, indicating that the CD moves as a result of the photoisomerisation. This is consistent with α-CD less readily accommodating a *cis*-azobenzene moiety than the *trans*-isomer.[15,35,36] The central methylene protons of the propyl groups of the rotaxane **19** give rise to resonances at δ 1.84 and 2.06 ppm in the 1D ^{1}H NMR spectrum, which are distinct due to the asymmetry imposed by the CD. These show NOE interactions with CD protons, indicating that at various times the CD is located over each propyl group. If the CD did not move between these two locations, there would be two distinct compounds with distinguishable spectra. Therefore, instead, it is logical to assume that the CD moves from one to the other propyl group, over the azobenzene moiety, on the NMR time-scale. The operation of the rotaxane **9a** as a photochemical molecular shuttle is therefore as illustrated in Fig. 4.

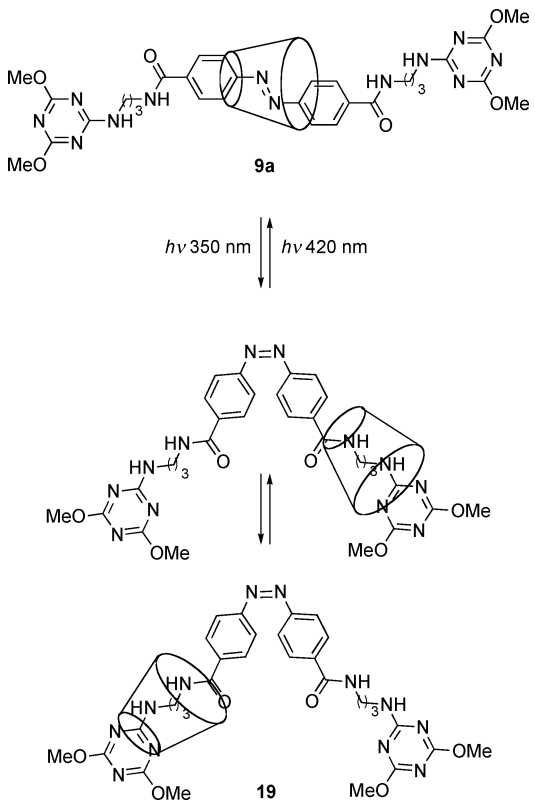


Fig. 4 Operation of the rotaxane **9a** as a photochemical molecular shuttle.

It follows that methoxytriazines are effective blocking groups for α-CD-based [2]-rotaxanes with alkane-, stilbene- and azobenzene-based axles. The capping reagents, 2-chloro-4,6-dimethoxy-1,3,5-triazine (**7**) and 2,4-dichloro-6-methoxy-1,3,5-triazine (**13**), both show the necessary selectivity to react with nucleophilic guests complexed by α-CD in aqueous solution, irrespective of whether the guest is an aliphatic or a less-reactive aromatic diamine. When the dichlorotriazine **13** is used, the triazinyl chlorines remaining in the rotaxanes may be displaced through further nucleophilic aromatic substitution, providing synthetic versatility, and the methoxytriazine-capped rotaxanes appear to be suitable for the construction of photochemical molecular devices.

Experimental

General

NMR spectra were recorded on either a Varian Gemini 300 spectrometer or a Varian Inova 500 spectrometer. Chemical shift (δ) values are given in ppm and coupling constants (J) are given in Hertz. MeOH-d_4 with an isotopic purity of 99.8% was purchased from Apollo Scientific Ltd. DMSO-d_6 with an isotopic purity of 99.8% and $CDCl_3$ with an isotopic purity of 99.8% were purchased from Cambridge Isotope Laboratories Inc. Electrospray ionisation (ESI) mass spectra were recorded using either a Micromass-Waters LC-ZMD single quadrupole liquid chromatograph mass spectrometer or a Bruker Apex 4.7 T FTICR mass spectrometer. Elemental analyses were performed by the Australian National University Analytical Services Unit based at the Research School of Chemistry. Melting points were determined on a Kofler hot-stage melting point apparatus under a Reichert microscope and are uncorrected. High performance liquid chromatography (HPLC) was performed using a Waters 600 Controller with a Waters 717 plus Autosampler, a Waters 2996 Photodiode Array Detector running with Empower Pro Empower 2 software, and a Waters Fraction Collector III. Thin layer chromatography (TLC) was carried out on alumina backed plates coated with Merck silica gel F_{254}. Developed plates were visualised using ultraviolet light and/or by dipping the plates into a solution of 0.1% naphthalene-1,3-diol in 200 : 157 : 43 v/v/v ethanol–water–H_2SO_4, followed by heating with a heat gun.[28,29] α-CD was acquired from Nihon Shokuhin Kako Co., Japan, in 99.1% purity and was dried over P_2O_5 under reduced pressure to constant weight before use. Diaion HP-20 resin was purchased from Supelco, PA. All other starting materials, solvents and reagents were commercially available.

[*N*,*N*′-Bis(4,6-dimethoxy-1,3,5-triazin-2-yl)-1,12-diaminododecane]-[α-cyclodextrin]-[2]-[rotaxane] (8)

A mixture of α-CD (1.80 g, 1.85 mmol) and the diamine **6** (77 mg, 0.38 mmol) in 0.2 mol dm^{-3} carbonate buffer (pH 10, 25 cm^3) was stirred at room temperature for 2 h, before the triazine **7** (0.27 g, 1.55 mmol) was added and that mixture was stirred at room temperature for an additional 12 h. The resulting solution was washed with EtOAc (5 × 25 cm^3) and concentrated under reduced pressure. The residue dissolved in water (40 cm^3) and the solution was applied to a Diaion HP-20 column (310 × 25 mm). The column was eluted with water (*ca.* 3.0 dm^3) until no more unreacted α-CD was detected by TLC. A water–methanol gradient was then applied to the column and fractions eluting with 30% aqueous methanol were combined and concentrated under reduced pressure, to give the title compound **8** as a colourless powder (140 mg, 25%); mp 203–204 °C (dec.); δ_H (500 MHz, MeOH-d_4) 4.98 (6H, d, J 3.5), 4.02–3.98 (6H, m), 3.94 (6H, s), 3.92 (6H, s), 3.88–3.86 (12H, m), 3.78–3.74 (6H, m), 3.59–3.51 (12H, m), 3.42–3.37 (4H, m), 1.71–1.60 (4H, m), 1.57–1.34 (16H, m); δ_C

(75.5 MHz, MeOH-d_4) 172.8, 172.2, 168.8, 168.5, 103.9, 83.3, 75.1, 73.7, 73.4, 61.4, 55.5, 55.2(3), 55.2, 55.1, 42.1, 42.0, 32.4, 32.3, 32.0, 31.9, 31.7, 31.0, 30.6, 30.3, 29.0, 28.2; *m/z* (ESI, positive) 1451 ($M + H^+$); TLC (5 : 4 : 3 v/v/v, *n*-BuOH–EtOH–H_2O) R_f 0.45 (relative to the solvent front), 1.7 (relative to α-CD); elemental analysis: found: C, 45.87; H, 6.44; N, 7.11. $C_{58}H_{98}N_8O_{34}\cdot 3H_2O$ requires C, 46.27; H, 6.96; N, 7.44%.

[(*E*)-*N*,*N*′-Bis(3-(4,6-dimethoxy-1,3,5-triazin-2-ylamino)propyl)-4,4′-azobenzenedicarboxamide]-[α-cyclodextrin]-[2]-[rotaxane] (9a)

A mixture of α-CD (3.0 g, 3.09 mmol) and the diamine **11** (0.10 g, 0.26 mmol) in 0.2 mol dm^{-3} carbonate buffer (pH 10, 25 cm^3) was stirred at room temperature for 2 h, before the triazine **7** (0.27 g, 1.55 mmol) was added and that mixture was stirred at room temperature for an additional 12 h. The resulting solution was washed with EtOAc (5 × 25 cm^3) and concentrated under reduced pressure. The residue dissolved in water (40 cm^3) and the solution was applied to a Diaion HP-20 column (310 × 25 mm). The column was eluted with water (*ca.* 3.0 dm^3) until no more unreacted α-CD was detected by TLC. A water–methanol gradient was then applied to the column and fractions eluting with 40% aqueous methanol were combined and concentrated under reduced pressure, to give the title compound **9a** as an orange powder (131 mg, 31%); mp 226–228 °C (dec.); δ_H (500 MHz, MeOH-d_4) 8.54 (2H, d, *J* 8.5), 8.12 (2H, d, *J* 8.5), 8.10 (2H, d, *J* 8.5), 7.96 (2H, d, *J* 8.5), 4.88 (6H, br), 3.97–3.92 (12H, m), 3.79–3.77 (6H, m), 3.74–3.70 (12H, m), 3.55–3.49 (20H, m), 3.44–3.41 (6H, m), 2.02–1.95 (4H, m); δ_C (75.5 MHz, MeOH-d_4) 185.1, 169.4, 169.1, 129.6, 128.8, 125.8, 123.9, 103.7, 82.8, 74.7, 73.5, 73.1, 61.3, 54.8, 39.2, 34.8, 30.0; *m/z* (ESI, positive) 1633 [($M + H^+$), 80], 1655 [($M + Na^+$), 100]; HPLC t_R 2.98 min [YMC-PACK ODS-AQ column (250 × 10 mm), eluting with H_2O–MeCN (3 : 1, v/v), flow rate 3.0 cm^3 min^{-1}]; TLC (5 : 4 : 3 : 2 v/v/v/v, *i*-PrOH–EtOH–H_2O–AcOH) R_f 0.75 (relative to the solvent front), 1.20 (relative to α-CD); elemental analysis: found: C, 44.85; H, 6.30; N, 9.10. $C_{66}H_{96}N_{12}O_{36}\cdot 8H_2O$ requires C, 44.59; H, 6.35; N, 9.46%.

[(*E*)-*N*,*N*′-Bis(3-(4-chloro-6-methoxy-1,3,5-triazin-2-ylamino)propyl)-4,4′-azobenzenedicarboxamide]-[α-cyclodextrin]-[2]-[rotaxane] (9b)

A mixture of α-CD (3.0 g, 3.09 mmol) and the diamine **11** (0.10 g, 0.26 mmol) in water (25 cm^3) adjusted to pH 10 with triethylamine was stirred at room temperature for 2 h, before the triazine **13** (0.34 g, 1.88 mmol) was added and that mixture was stirred at room temperature for an additional 12 h. The resulting solution was washed with EtOAc (5 × 25 cm^3) and concentrated under reduced pressure. The residue dissolved in water (40 cm^3) and the solution was applied to a Diaion HP-20 column (310 × 25 mm). The column was eluted with water (*ca.* 3.0 dm^3) until no more unreacted α-CD was detected by TLC. A water–methanol gradient was then applied to the column and fractions eluting with 20–30% aqueous methanol were combined and concentrated under reduced pressure. HPLC of the residue gave the title compound **9b** as an orange powder (20 mg, 5%); mp 252–256 °C (dec.); δ_H (500 MHz, DMSO-d_6) 8.80 (1H, t, *J* 4.5), 8.34 (2H, d, *J* 8.0), 8.07–8.06 (4H, m), 7.93 (2H, d, *J* 8.0), 7.95–7.90 (1H, m), 7.72 (2H, d, *J* 8.0), 5.34–5.33 (6H, m), 5.31–5.30 (6H, m), 4.69 (6H, d, *J* 3.3), 4.39–4.37 (6H, m), 3.84–3.80 (6H, m), 3.55–3.35 (24H, m), 3.25–3.24 (6H, m), 3.20–3.18 (14H, m), 1.86–1.79 (4H, m); δ_C (75.5 MHz, MeOH-d_4) 172.5, 172.0, 171.9, 171.2, 170.0, 169.1, 168.4, 154.9, 154.7, 139.2, 138.6, 129.8, 129.1, 126.2, 126.1, 124.2, 103.9, 83.1, 75.0, 73.8, 73.4, 61.7, 55.9, 55.7, 42.1, 39.7, 30.1, 30.0; *m/z* (ESI, positive) 1642 [($M + H^+$), 10], 1664 [($M + Na^+$), 100]; TLC (5 : 4 : 3 : 2 v/v/v/v, *i*-PrOH–EtOH–H_2O–AcOH) R_f 0.75 (relative to the solvent front), 1.30 (relative to α-CD); HPLC t_R 6.5 min [Luna Phenomenex column (250 × 10 mm), eluting with H_2O–MeCN–TFA (70 : 30 : 0.1, v/v/v), flow rate 3.0 cm^3 min^{-1}]; elemental analysis: found: C, 44.44; H, 5.74; N, 9.95. $C_{64}H_{90}Cl_2N_{12}O_{34}.5H_2O$ requires C, 44.37; H, 5.82; N, 9.70%.

[(*E*)-*N*,*N*′-Bis(3-(4-allylamino-6-methoxy-1,3,5-triazin-2-ylamino)propyl)-4,4′-azobenzenedicarboxamide]-[α-cyclodextrin]-[2]-[rotaxane] (9c)

To a solution of the [2]-rotaxane **9b** (20 mg, 10 μmol) in anhydrous DMF (1 cm^3), allylamine (1 cm^3) was added, and the mixture was left stirring for 10 h at room temperature, before it was added dropwise to acetone (10 cm^3). The resultant precipitate was collected by centrifugation and resuspended in acetone (15 cm^3). The solid was collected, again by centrifugation. HPLC of this material gave the title compound **9c** as an orange powder (12 mg, 59%); mp 270–274 °C (dec.); δ_H (500 MHz, MeOH-d_4) 8.58–8.52 (2H, m), 8.13–8.09 (4H, m), 7.99–7.96 (2H, d, *J* 8.0), 5.21 (2H, m), 5.09 (4H, m), 4.98 (6H, m), 4.02 (3H, s), 3.93 (3H, s), 3.78–3.70 (20H, m), 3.68–3.56 (16H, m), 3.55–3.50 (6H, m), 3.52–3.50 (6H, m), 2.16–1.97 (4H, m); δ_C (75.5 MHz, MeOH-d_4) 178.3, 172.1, 168.2, 154.9, 136.4, 129.9, 129.1, 124.2, 115.8, 103.9, 83.1, 75.0, 73.8, 73.3, 61.7, 54.3, 44.0, 39.2, 35.4, 30.5; *m/z* (ESI, positive) 1683 ([$M + H^+$), 100], 1705 [($M + Na^+$), 50]; TLC (5 : 4 : 3 : 2 v/v/v/v, *i*-PrOH–EtOH–H_2O–AcOH) R_f 0.85 (relative to the solvent front), 1.15 (relative to α-CD); HPLC t_R 9.2 min [Luna Phenomenex column (250 × 10 mm), eluting with H_2O–MeCN–TFA (85 : 15 : 0.1, v/v/v), flow rate 3.0 cm^3 min^{-1}]; elemental analysis: found: C, 45.47; H, 6.28; N, 10.53. $C_{70}H_{102}N_{14}O_{34}.9H_2O$ requires C, 45.55; H, 6.55; N, 10.62%.

[(*E*)-*N*,*N*′-Bis(4,6-dimethoxy-1,3,5-triazin-2-yl)-4,4′-diaminostilbene]-[α-cyclodextrin]-[2]-[rotaxane] (10)

A mixture of α-CD (0.69 g, 0.71 mmol) and the stilbene **1** (50 mg, 0.24 mmol) in water (80 cm^3) adjusted to pH 9 with triethylamine was stirred at room temperature for 2 h, before the triazine **7** (88 mg, 0.50 mmol) was added and that mixture was stirred at room temperature for an additional 17 h. The resulting solution was washed with EtOAc (3 × 50 cm^3) and concentrated under reduced pressure. HPLC of the residue gave the title compound **10** as an colourless powder (17 mg, 5%); mp 264 °C (dec.); δ_H (500 MHz, DMSO-d_6) 10.23 (1H, s), 9.94 (1H, s), 7.75–7.78 (4H, m), 7.74 (2H, d, *J* 8.0), 7.22 (2H, d, *J* 8.0), 6.98 (1H, d, *J* 16.0), 6.79 (1H, d, *J* 16.0), 5.42 (6H, s), 5.28 (6H, s), 4.75 (6H, d, *J* 2.5), 4.41 (6H, apparent t, *J* 5.5), 3.88–3.98 (12H, m), 3.70 (6H, apparent d, *J* 9.5), 3.65 (6H, apparent t, *J* 9.0), 3.59 (6H, m), 3.43 (6H, apparent t, *J* 9.0), 3.30 (6H, m), 3.24 (6H, m); δ_C (125 MHz, DMSO-d_6) 173.0–171.8 (br), 165.8, 165.7, 138.0, 137.7, 133.5, 131.4, 131.0, 127.5, 127.3, 125.8, 125.2, 120.1, 119.7, 102.1, 81.7, 73.2, 72.1, 71.8,

61.0, 54.2–55.8 (br); *m/z* (ESI, positive) 1462 ($M + H^+$); TLC (5 : 4 : 3 v/v/v, *n*-butanol–ethanol–water) R_f 0.55 (relative to the solvent front), 1.15 (relative to α-CD); HPLC t_R 13.6 min [YMC-PACK ODS-AQ column (250 × 20 mm), eluting with H_2O–MeCN (9 : 1, v/v), flow rate 10.0 cm^3 min^{-1}]; elemental analysis: found: C, 43.70; H, 6.13; N, 6.60. $C_{60}H_{84}N_8O_{34}.10H_2O$ requires C, 43.90; H, 6.39; N, 6.83%.

(*E*)-*N*,*N*′-Bis(3-aminopropyl)-4,4′-azobenzenedicarboxamide (11)

A solution of Boc_2O (6.0 g, 28 mmol) in $CHCl_3$ (38 cm^3) was added dropwise to a solution of 1,3-diaminopropane (138 cm^3) in $CHCl_3$ (250 cm^3) at 0 °C, then the mixture was allowed to warm to room temperature and stirred for 2 h, before it was filtered and the filtrate was concentrated under reduced pressure. The oily residue was dissolved in EtOAc (125 cm^3) and the solution was washed with brine, dried ($MgSO_4$) and allowed to evaporate over 2 weeks, to form *N*-(*tert*-butoxycarbonyl)-1,3-diaminopropane as a colourless solid (2.4 g, 50%); mp 94–96 °C; δ_H (300 MHz, $CDCl_3$) 4.93 (1H, s), 3.21–3.15 (2H, m), 2.76–2.71 (2H, m), 1.71 (9H, s), 1.63–1.54 (2H, m), 1.41 (2H, m); *m/z* (ESI, positive) 175 ($M + H^+$).

(*E*)-4,4′-Azobenzenedicarboxylic acid (0.10 g, 0.37 mmol), *N*-(*tert*-butoxycarbonyl)-1,3-diaminopropane (0.15 g, 0.88 mmol) and BOP (0.39 g, 0.89 mmol) were dissolved in anhydrous DMF (4 cm^3). Triethylamine (0.13 cm^3) was added and the mixture was stirred for 12 h at room temperature. The resultant precipitate was separated by filtration and recrystallised from ethanol to yield (*E*)-*N*,*N*′-bis(3-(*tert*-butoxycarbonylamino)propyl)-4,4′-azobenzenedicarboxamide as an orange solid (0.20 g, 93%); mp 260–261 °C (dec.); δ_H (300 MHz, DMSO-d_6) 8.66 (2H, t, *J* 5.7), 8.05 (4H, d, *J* 8.0), 7.98 (4H, d, *J* 8.0), 6.85 (2H, t, *J* 5.5), 3.30–3.26 (4H, m), 3.01–2.95 (4H, m), 1.66–1.62 (4H, m), 1.37 (18H, s); δ_C (75.5 MHz, DMSO-d_6) 165.4, 155.7, 153.2, 137.1, 128.6, 122.6, 77.6, 37.8, 37.2, 29.6, 28.3; *m/z* (ESI, positive) 583 [($M + H^+$) 95], 605 [($M + Na^+$), 100]; elemental analysis: found: C, 61.51; H, 6.99; N, 14.23. $C_{30}H_{42}N_6O_6$ requires C, 61.84; H, 7.26; N, 14.42%.

(*E*)-*N*,*N*′-Bis(3-(*tert*-butoxycarbonylamino)propyl)-4,4′-azobenzenedicarboxamide (0.19 g, 0.33 mmol) was dissolved in 4 mol dm^{-3} HCl in dioxane (8 cm^3) and the solution was stirred for 2 h at room temperature. The resultant precipitate was separated by filtration and redissolved in saturated aqueous sodium hydroxide (75 cm^3). That solution was extracted with EtOAc (3 × 50 cm^3) and the combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure to afford the title compound **11** as an orange powder (0.12 g, 95%); mp 280–282 °C (dec.); δ_H (300 MHz, DMSO-d_6) 8.97 (2H, t, *J* 5.5), 8.11 (4H, d, *J* 8.5), 7.99 (4H, d, *J* 8.5), 3.38–3.35 (8H, m), 2.88–2.81 (4H, m), 1.90–1.82 (4H, m); δ_C (75.5 MHz, DMSO-d_6) 165.6, 153.3, 136.8, 128.6, 122.6, 36.8, 36.4, 27.3; *m/z* (ESI, positive) 383 [($M + H^+$) 100], 405 [($M + Na^+$), 15]; elemental analysis: found: C, 52.36; H, 6.28; N, 18.22. $C_{20}H_{26}N_6O_2 \cdot 2HCl$ requires C, 52.75; H, 6.20; N, 18.45%.

[(*E*)-*N*,*N*′-Bis(4-chloro-6-methoxy-1,3,5-triazin-2-yl)-4,4′-diaminostilbene]-[α-cyclodextrin]-[2]-[rotaxane] (14a)

A mixture of α-CD (0.69 g, 0.71 mmol) and the stilbene **1** (50 mg, 0.24 mmol) in water (80 cm^3) adjusted to pH 9 with triethylamine was stirred at room temperature for 2 h, before the triazine **13** (90 mg, 0.50 mmol) was added and that mixture was stirred at room temperature for an additional 17 h. The resulting solution was washed with EtOAc (3 × 50 cm^3) and concentrated under reduced pressure. HPLC of the residue gave the title compound **14a** as an colourless powder (69 mg, 20%); mp 265 °C (dec.); δ_H (500 MHz, DMSO-d_6) 10.81 (1H, s), 10.62 (1H, s), 7.80 (2H, d, *J* 7.5), 7.76 (2H, d, *J* 7.5), 7.71 (2H, d, *J* 7.5), 7.27 (2H, d, *J* 7.5), 7.02 (1H, d, *J* 16.5), 6.83 (1H, d, *J* 16.5), 4.75 (6H, d, *J* 2.5), 4.04 (3H, s), 4.00 (3H, s), 3.56–3.69 (18H, m), 3.43 (6H, apparent t, *J* 4.0), 3.29 (6H, m), 3.23 (6H, dd, *J* 3.0, 12.5); *m/z* (ESI, positive) 1492 ($M + Na^+$); TLC (5 : 4 : 3 v/v/v, *n*-BuOH–EtOH–H_2O) R_f 0.70 (relative to the solvent front), 1.80 (relative to α-CD); HPLC t_R 10.8 min [YMC-PACK ODS-AQ column (250 × 20 mm), eluting with H_2O–MeCN (7 : 1, v/v), flow rate 10.0 cm^3 min^{-1}]; elemental analysis: found: C, 42.87; H, 5.69; N, 6.61. $C_{58}H_{78}Cl_2N_8O_{32} \cdot 9H_2O$ requires C, 42.68; H, 5.93; N, 6.86%.

[(*E*)-*N*,*N*′-Bis(4-chloro-6-methoxy-1,3,5-triazin-2-yl)-4,4′-azobenzenedicarboxamide]-[α-cyclodextrin]-[2]-[rotaxane] (14b)

A mixture of α-CD (3.0 g, 3.1 mmol) and the azobenzene **12** (100 mg, 0.47 mmol) in water (25 cm^3) adjusted to pH 10 with triethylamine was stirred at room temperature for 2 h, before the triazine **13** (0.34 g, 1.9 mmol) was added and that mixture was stirred at room temperature for an additional 12 h. The resulting solution was washed with EtOAc (5 × 25 cm^3) and concentrated under reduced pressure.

The residue dissolved in water (40 cm^3) and the solution was applied to a Diaion HP-20 column (310 × 25 mm). The column was eluted with a water–methanol solvent gradient and fractions eluting with 20–30% aqueous methanol were combined and concentrated under reduced pressure. HPLC of the residue gave the title compound **14b** as an orange powder (128 mg, 19%); mp 262–265 °C (dec.); δ_H (500 MHz, MeOH-d_4) 8.46 (2H, d, *J* 8.5), 8.09 (2H, d, *J* 8.5), 7.96 (2H, d, *J* 8.5), 7.80 (2H, d, *J* 8.5), 4.92 (6H, d, *J* 3.5), 4.13 (3H, s), 4.10 (3H, s), 3.85–3.70 (18H, m), 3.60–3.45 (18H, m); δ_C (75.5 MHz, MeOH-d_4) 166.4, 166.2, 149.6, 149.1, 142.2, 126.6, 124.2, 121.7, 103.5, 82.7, 74.9, 73.4, 73.3, 73.2, 72.9, 61.2; *m/z* (ESI, positive) 1493 ($M + Na^+$); TLC (5 : 4 : 3 v/v/v, *n*-BuOH–EtOH–H_2O) R_f 0.50 (relative to the solvent front), 4.0 (relative to α-CD); HPLC: t_R 21.0 min [Luna Phenomenex column (250 × 10 mm), eluting with H_2O–MeCN (9 : 1, v/v), flow rate 3.0 cm^3 min^{-1}]; elemental analysis: found: C, 41.75; H, 5.82; N, 8.70. $C_{56}H_{76}Cl_2N_{10}O_{32}.7H_2O$ requires C, 42.08; H, 5.68; N, 8.76%.

[(*E*)-*N*,*N*′-Bis(4-phenylamino-6-methoxy-1,3,5-triazin-2-yl)-4,4′-diaminostilbene]-[α-cyclodextrin]-[2]-[rotaxane] (16a)

A solution of the [2]-rotaxane **14a** (30 mg, 20 μmol) in 50% aqueous acetonitrile (10 cm^3) was adjusted to pH 9 with triethylamine, before aniline (19 mg, 20 μmol) was added and the mixture was stirred at 50 °C for 3 h. HPLC of the crude product obtained by concentration of the reaction mixture under reduced pressure gave the title compound **16a** as a colourless powder (11 mg, 33%); δ_H (500 MHz; DMSO-d_6) 9.81 (1H, s), 9.71 (1H, s), 9.47 (2H, s), 7.83 (4H, d, *J* 7.5), 7.80–7.75 (6H, m), 7.31 (4H, t, *J* 7.5), 7.16 (2H, m), 7.00 (2H, t, *J* 7.5), 6.88 (2H, m), 5.44 (6H, s), 5.31 (6H, s), 4.77 (6H, d, *J* 3.0), 4.45 (6H, t, *J* 5.0), 3.94 (6H, s), 3.70–3.73

(12H, m), 3.61 (6H, m), 3.47 (6H, apparent t, *J* 4.0), 3.32 (6H, m), 3.26 (6H, m); δ_C (500 MHz, DMSO-d_6) 170.8, 164.9, 128.5, 125.7, 120.1, 102.1, 81.6, 73.2, 72.2, 71.8, 59.2, 54.0; *m/z* (ESI, positive) 1583.578 (M + H^+) (calculated for $C_{70}H_{90}N_{10}O_{32}$ *m/z* 1583.580); TLC (5 : 4 : 3 v/v/v, *n*-BuOH–EtOH–H_2O) R_f 0.75 (relative to the solvent front), 2.1 (relative to α-CD); HPLC t_R 18.9 min [YMC-PACK ODS-AQ column (250 × 20 mm), eluting with H_2O–MeCN (3 : 1, v/v), flow rate 10.0 cm^3 min^{-1}]; elemental analysis: found: C, 46.74; H, 6.45; N, 7.52. $C_{70}H_{90}N_{10}O_{32}\cdot 12H_2O$ requires C, 46.72; H, 6.38; N, 7.78%.

[(*E*)-*N*,*N*′-Bis(4-(3-aminopropylamino)-6-methoxy-1,3,5-triazin-2-yl)-4,4′-azobenzenedicarboxamide]-[α-cyclodextrin]-[2]-[rotaxane] (16b)

To a solution of the [2]-rotaxane **14b** (25 mg, 17 μmol) in anhydrous DMF (1 cm^3), 1,3-diaminopropane (2.8 μm^3, 40 μmol) was added, and the mixture was left stirring for 10 h at room temperature, before it was added dropwise to acetone (10 cm^3). The resultant precipitate was collected by centrifugation and resuspended in acetone (15 cm^3). The solid was collected, again by centrifugation. HPLC of this material gave the title compound **16b** as an orange powder (20 mg, 76%); mp 282–285 °C (dec.); δ_H (500 MHz, MeOH-d_4) 8.47 (2H, d, *J* 8.5), 8.03 (2H, d, *J* 8.5), 7.94 (2H, d, *J* 8.5), 7.85 (2H, d, *J* 8.5), 4.90 (6H, d, *J* 3.5), 4.13 (3H, s), 4.10 (3H, s), 3.81–3.73 (18H, m), 3.55–3.49 (26H, m), 2.07–2.00 (4H, m); δ_C (75.5 MHz, MeOH-d_4) 166.4, 166.2, 126.6, 124.4, 121.9, 121.5, 117.2, 103.9, 83.2, 75.0, 75.9, 73.3, 73.2, 72.9, 61.2, 37.0, 36.0, 28.7; *m/z* (ESI, positive) 1548 (M + H^+); TLC (5 : 4 : 3 : 2 v/v/v/v, *i*-PrOH–EtOH–H_2O–AcOH) R_f 0.45 (relative to the solvent front), 0.56 (relative to the [2]-rotaxane **14b**); HPLC t_R 5.2 min [Luna Phenomenex column (250 × 10 mm), eluting with H_2O–MeCN–TFA (85 : 15 : 0.1, v/v/v), flow rate 3.0 cm^3 min^{-1}].

[(*E*)-6^A^-*O*-(*N*-(4-chloro-6-methoxy-1,3,5-triazin-2-yl))-4′-aminostilben-4-yl-[α-cyclodextrin]-[c_2]-[daisy chain] (18)

A mixture of the cyclodextrin derivative **17** (52 mg, 46 μmol) in 0.2 mol dm^{-3} carbonate buffer (pH 10, 3 cm^3) was stirred at room temperature for 5 h, before the triazine **13** (8 mg, 44 μmol) was added and that mixture was stirred at room temperature for an additional 10 h. HPLC of the crude product obtained by concentration of the reaction mixture under reduced pressure gave the title compound **18** as a tan powder (14 mg, 12%); mp 266–268 °C (dec.); δ_H (500 MHz, DMSO-d_6) 10.54 (2H, s), 7.94 (4H, d, *J* 8.0), 7.87 (4H, d, *J* 8.0), 7.28 (4H, d, *J* 8.0), 7.04 (2H, d, *J* 15.5), 6.90 (2H, d, *J* 15.5), 6.65 (4H, d, *J* 8.0), 5.76–5.22 (12H, m), 4.87–3.04 (112H, m); δ_C (125 MHz, DMSO-d_6) 171.1, 169.5, 164.3, 157.6, 136.5, 132.3, 128.6, 127.5, 126.7, 126.0, 125.9, 120.3, 113.9, 102.3, 102.0, 101.8, 101.2, 83.1, 82.0, 81.8, 81.4, 73.6, 73.4, 73.3, 73.0, 73.0, 72.9, 72.6, 72.4, 72.2, 72.0, 71.9, 71.7, 71.5, 71.4, 71.2, 68.9, 66.4, 59.6, 59.3; *m/z* (ESI, positive) 2658 (M + K^+); TLC (5 : 4 : 3 v/v/v, *n*-BuOH–EtOH–H_2O) R_f 0.3 (relative to the solvent front); HPLC t_R 14.9 min [YMC-PACK ODS-AQ column (250 × 10 mm), eluting with H_2O–MeCN (19 : 1, v/v), flow rate 3.0 cm^3 min^{-1}]; elemental analysis: found: C, 43.51; H, 6.22; N, 3.75. $C_{108}H_{146}Cl_2N_8O_{62}\cdot 20H_2O$ requires C, 43.54; H, 6.29; N, 3.76%.

[(*Z*)-*N*,*N*′-Bis(3-(4,6-dimethoxy-1,3,5-triazin-2-ylamino)propyl)-4,4′-azobenzenedicarboxamide]-[α-cyclodextrin]-[2]-[rotaxane] (19)

A solution of the *trans*-azobenzene-based rotaxane **9a** (30 mg, 18 μmol) in water (0.6 dm^3) in a quartz reaction vessel was irradiated at 350 nm in a Luzchem photochemical reactor for 0.25 h, before it was concentrated under reduced pressure to a volume of 3 cm^3. HPLC of this solution afforded a 65 : 35 mixture of the title compound **19** and the *trans*-isomer **9a** as an orange powder (12 mg, 40%). The title compound **19** showed: δ_H (500 MHz, MeOH-d_4) 7.83 (2H, d, *J* 8.5), 7.75 (2H, d, *J* 8.5), 6.95 (4H, d, *J* 8.5), 2.08–2.07 (2H, m), 1.89–1.87 (2H, m); HPLC t_R 3.74 min [YMC-PACK ODS-AQ column (250 × 10 mm), eluting with H_2O–MeCN (3 : 1, v/v), flow rate 3.0 cm^3 min^{-1}].

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