Centrosymmetric and non-centrosymmetric packing of aligned molecular fibres in the solid state self assemblies of cyclodextrin-based rotaxanes

Marta M. Cieslinski,[a] Peter J. Steel,[b] Stephen F. Lincoln,[c] Christopher J. Easton[a]

[a] Research School of Chemistry, Institute of Advanced Studies

Australian National University

Canberra ACT 0200 (Australia)

[b] Department of Chemistry, University of Canterbury

Christchurch (New Zealand)

[c] School of Chemistry and Physics, University of Adelaide

Adelaide, SA 5005 (Australia)

Abstract:

Two [2]-rotaxanes each comprising α-cyclodextrin as the rotor, and with either 3,3'-difluoro- or 3,3'-dichloro-stilbene as the axle and trinitrophenylamino substituents as the blocking groups at the 4- and 4'-positions were prepared and their structures analyzed in solution and the solid-state

using ^{1}H NMR spectroscopy and X-ray crystallography, respectively. With each rotaxane, in solution the stilbene rotates freely within the cyclodextrin annulus. In the solid state the 3,3'-dichlorostilbene-based rotaxane adopts two very similar conformations, each having the chlorines in the *syn,syn*-orientation. By comparison the 3,3'-difluorostilbene-based rotaxane adopts *syn,syn*-, *syn,anti*- and *anti,anti*-orientations of the substituents. The crystal packing of each rotaxane displays aligned molecular fibres, which are centrosymmetrically oriented in the case of the difluoride due to the head-to-head / tail-to-tail alignment of the cyclodextrins. By contrast all of the cyclodextrins in the dichloride are aligned head-to-tail along a single axis to give a polar, non-centrosymmetric crystal.

Introduction:

Rotaxanes consist of macrocycles encompassing axles that are capped with blocking groups to prevent the components from dissociating.(REF1) Cyclodextrin-based rotaxanes have been prepared and used as molecular shuttles and photochemical and mechanical devices.(REF2,3,4,5) Our interest in this area has been focused on α-cyclodextrin-based rotaxanes with stilbenes as the axles and trinitrophenyl blocking groups, as the basis of molecular machines and new materials(REF3,4). In particular we recently reported the synthesis of the rotaxanes **1** and **2** and studies of their solution and solid state structures.(REF4) In the solid state self assemblies the dumbbells of these species form aligned molecular fibres separated by the cyclodextrins.   These resemble the insulated molecular wires with reduced interstrand interactions reported by Anderson *et al.*,(REF5) in their studies of rotaxanes and polyrotaxanes.

In those cases the structures are associated with unusual physical, electronic and photochemical properties.

In order to better understand the cooperative molecular recognition events that result in the ordered networks seen in the solid state structures of the rotaxanes **1** and **2**, we have now prepared and studied the corresponding difluoride **3** and dichloride **4**. Each of these retains the molecular fibre structural motif observed with the rotaxanes **1** and **2** but whereas the crystal packing of the rotaxanes **1-3** is centrosymmetric, that of the dichloride **4** is non-centrosymmetric with all of the cyclodextrins aligned head-to-tail along a single axis. Non-centrosymmetric crystals are of considerable interest due to their potential for application, for example in optics and optoelectronics.(REF6)
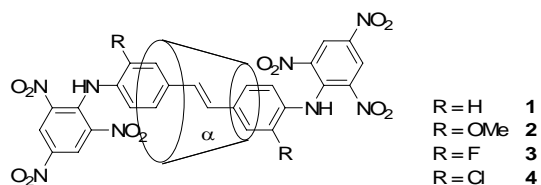
Results and Discussion:

The rotaxane **3** was prepared as outlined in Scheme 1. The procedure used to prepare the stilbene precursors to the rotaxanes **1** and **2** involved treatment of nitrotoluenes with oxygen under strongly basic conditions. When the same approach was attempted with 3-fluoro-4-nitrotoluene to prepare 3,3'-difluoro-4,4'-dinitrostilbene, instead 3,3'-dihydroxy-4,4'-dinitrostilbene was obtained. Therefore the alternative approach reported by Jeffery and Ferber(REF7) was adopted. Accordingly 2-fluoro-4-iodoaniline **5** was converted to the corresponding acetamide **6**, which underwent palladium-catalyzed condensation with

vinyltrimethylsilane to give the stilbene **7**. Hydrolysis then afforded the diaminostilbene **8**. The

stilbene **8** was stirred with α-cyclodextrin **12** for 16 hours in aqueous buffer at room temperature

and pH 10, to allow the stilbene **8** to dissolve and the inclusion complex **13** to form. Sodium

2,4,6-trinitrobenzene-1-sulfonate **15** was then added and the mixture was stirred for an additional

4 hours. The crude product mixture was subjected to a Diaion HP-20 column and then HPLC to

give the rotaxane **3** as an orange powder in 73% yield. TLC of this material revealed a single

component, showing the characteristic ultraviolet absorbance of the dumbbell, and pink

colouration of a cyclodextrin on exposure to acidic naphthalene-1,3-diol.(REF8) The

deprotonated molecular ion of the product **3** was seen at *m/z* 1639 by ESI-MS operated in the

negative ion mode.
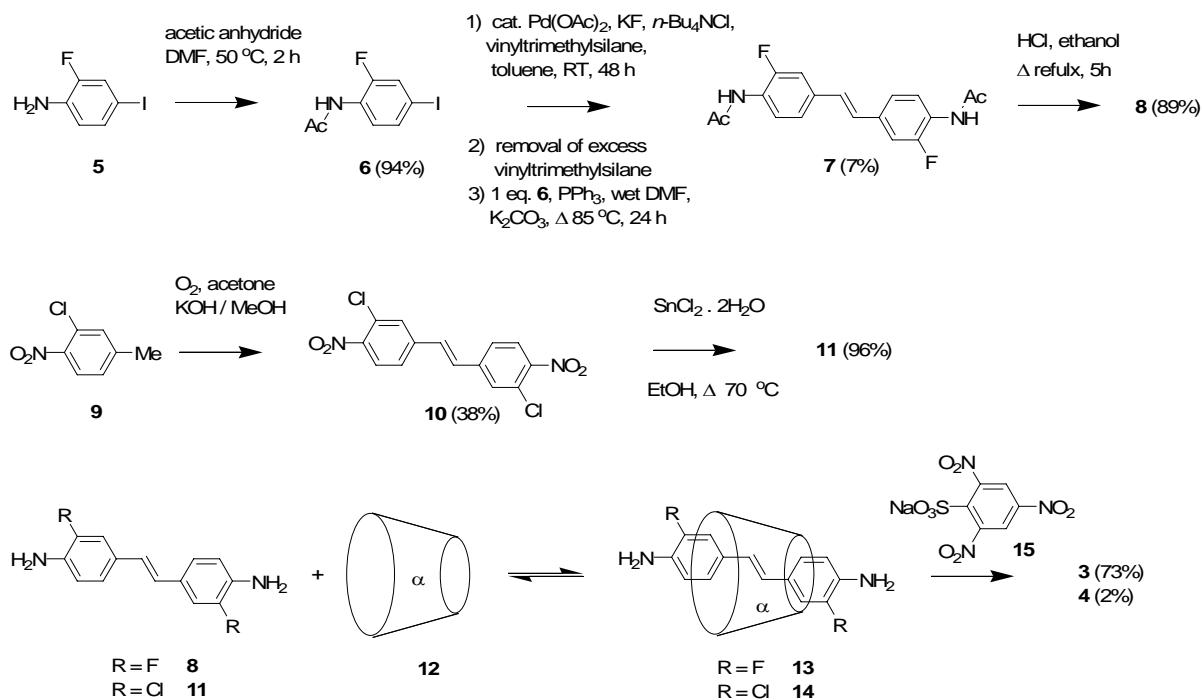
Scheme 1.

The ^{1}H NMR spectrum of the rotaxane **3** revealed the proton resonances of the cyclodextrin, the stilbene and the blocking groups. The cyclodextrin proton resonances for each glucopyranose unit were equivalent indicating symmetry of the cyclodextrin and therefore free rotation of the axle within the cavity on the NMR time-scale.

2D NMR techniques (ROESY, COSY and TOCSY) were employed for the assignment of the proton resonances of the rotaxane **3**, which were then used to analyze the conformation. Figure 1a) is a portion of the ROESY spectrum showing cross-peaks between cyclodextrin and stilbene proton resonances. The cyclodextrin is centred on the stilbene as the axle protons designated A-H2-H6 and H8 show strong interactions with the cyclodextrin protons CD-H3 and H5 whereas protons A-H7 and H1 found on the ends of the stilbene only show weak interactions with CD-H6 and H3 respectively.

The rotaxane **4** was prepared using a method similar to that used to obtain the rotaxane **3** (Scheme 1). The stilbene **11** was obtained as reported, by oxidative dimerization of 3-chloro-4-nitrotoluene **9**, followed by reduction of the dinitrostilbene **10**.(REF9) Due to the low solubility of this material, sonication was used to suspend and dissolve it in solution with α-cyclodextrin **12**. The crude product was subjected to a Diaion HP-20 column and then HPLC to give the rotaxane **4** as an orange powder, but in only 2% yield. The deprotonated molecular ion of the product **4** was seen at *m/z* 1671 by ESI-MS operated in the negative ion mode. Despite repeated attempts the yield was not improved. This poor yield is probably a result of the low thermodynamic stability of the inclusion complex **14** due to the relatively large size of the chloro substituents. By comparison the yields of the rotaxanes **1** and **3** were 79%(REF 4) and 73%, respectively, while that of the dimethoxide **2** was 27%(REF4).
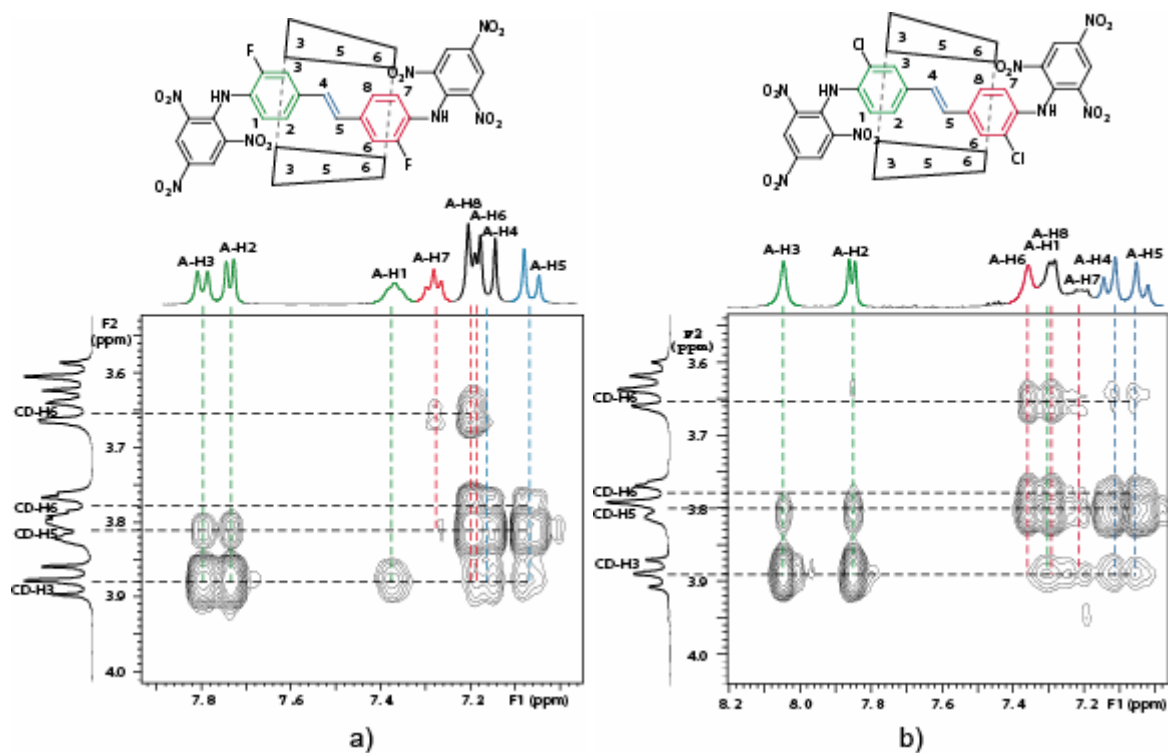
Figure 1. Sections of the 500 MHz ROESY spectra of a) the difluoro rotaxane **3** and b) the dichloride **4** in methanol-d_4 at 25 °C showing the region where cross-peaks between cyclodextrin and axle proton resonances are found.

Similar to that of the rotaxane **3**, the ^{1}H NMR spectrum of the rotaxane **4** reveals only one set of glucopyranose resonances indicating free rotation of the cyclodextrin around the stilbene axle. From the ROESY spectrum (Figure 1b)) the conformation can be determined. The cyclodextrin is centred over the stilbene as indicated by the intense cross peaks between the resonances of the axle protons designated A-H2-H6 and H8 and those of the cyclodextrin protons CD-H3, H5 and H6. It is apparent that the stilbene is 'tilted', rotating at an angle to the C_6-axis of the cyclodextrin. This is shown by, for example, the stronger interaction of CD-H5 and H6 with A-H2 than H3. Presumably this is a result of the bulkiness of the chlorines which forces them away from the sides of the cyclodextrin and pushes proton A-H2 further into the cyclodextrin cavity than A-H3.

To extend the study of the effect of various halogens, the synthesis of brominated analogues of the rotaxanes **3** and **4** was attempted. Based on the poor yield of the rotaxane **4** it was believed that the corresponding dibromide would not form due to the greater bulk of bromine relative to chlorine. Instead post-assembly rotaxane modification was attempted. Electrophilic aromatic bromination using pyridinium dichlorobromate(REF12) was envisaged as a way to introduce bromine at the 3- and 3'-positions of the stilbene of the rotaxane **1** based on the chemistry explored by Dumanski *et al.*(REF10) However such reactions yielded complex mixtures of products. When components were separated and analyzed by ^{1}H NMR spectroscopy, in most cases there was no evidence of olefinic proton resonances, indicating that addition had occurred across the double bond. One of the components was tentatively assigned as compound **16** based on 2D NMR spectroscopy and mass spectrometric studies.

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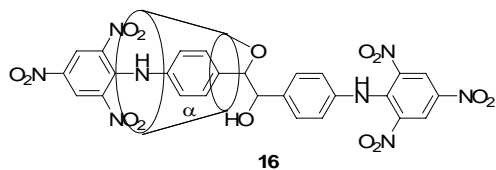
The solid state structures of the rotaxanes **3** and **4** were examined using X-ray crystallography. Crystals of each of the rotaxanes **3** and **4** were grown by slow evaporation of methanol-d_4 / D_2O solvent over a period of several weeks. In each case the asymmetric unit of the unit cell contains two independent molecules of the rotaxane **3** or **4** together with numerous solvent molecules. When there are substituents on the 3- and 3'-positions of a stilbene, three low-energy rotamers are possible, as shown in Figure 2.(REF11) Both of the two independent molecules of the dichloride **4** show the *syn,syn*-conformation. One of those in the asymmetric unit of the difluoride **3** shows disorder between the *syn,anti*- and *anti,anti*-conformations, while the other has the *syn,syn*-orientation. It could be that the *syn,syn*-conformation is favoured for the

dichloride **4** because this has the 3,3'-substituents furthest apart, as required for the accommodation within the cyclodextrin, which has an annular depth of approximately 8 Å.
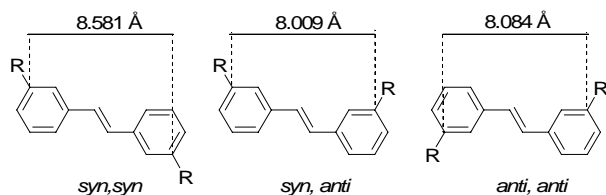

Figure 2. Possible rotamers of a 3,3'-disubstituted stilbene showing the average distances between the 3- and 3'-carbons as measured in the crystal structures of the rotaxanes **1-4**.

The conformations adapted by the dumbbells of the rotaxanes **1-4** are all very similar, with the trinitophenyl groups twisted at an angle to the pseudo-planar stilbene moieties (Figure 3). In principle these groups can be *syn* or *anti* with respect to the double bond. In practice the alignment in the rotaxane **3** was found to be *syn*, as observed for the rotaxanes **1** and **2**, but for the rotaxane **4** the blocking groups adopt the *anti* conformation. It is likely that the chlorines of the rotaxane **4** are too bulky to allow the crystallization of the blocking groups in the same way as for the other rotaxanes **1-3**.
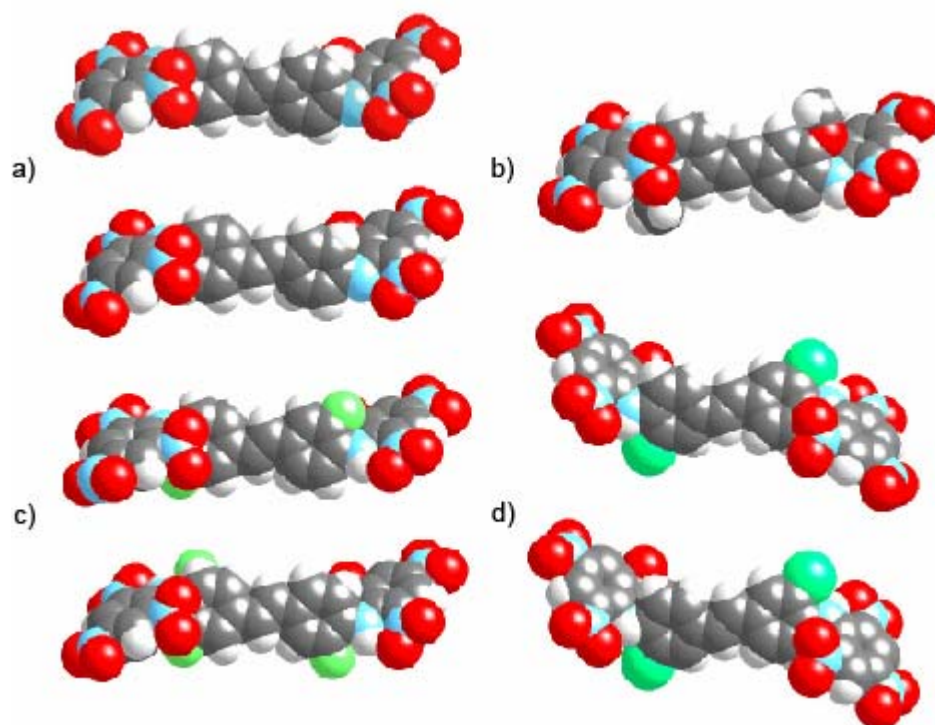
Figure 3. Conformations of the dumbbells in the crystals of a) the rotaxane **1**, b) the dimethoxide **2**, c) the difluoride **3** and d) the dichloride **4**, showing the alignment of the blocking groups. The atoms are shown with their Van der Walls radii where grey = carbon, red = oxygen, white = hydrogen, blue = nitrogen, light green = fluorine and dark green = chlorine.

Despite the different conformation of the blocking groups in the dichloride **4**, the crystal packing of all four rotaxanes **1-4** reveals strikingly similar molecular fibres, where the structural motif appears to be dominated by the intermolecular interactions between the trinitrophenyl substituents (Figure 4). In each case the fibres are aligned along a single axis with the dumbbells insulated by the cyclodextrins. In the absence of the cyclodextrin the molecule corresponding to the dumbbell of the rotaxane **1** also forms similar fibres in the crystal structure but these are neither all aligned nor insulated.(REF4)

Overall the crystal packing of the rotaxanes **1** and **3** is pseudo-centrosymmetric with the cyclodextrins orientated in a head-to-head / tail-to-tail fashion along the aligned molecular fibres

(Figures 4 a) and c)). Consequently these crystals are non-polar. In contrast, the cyclodextrins of the rotaxanes **2** and **4** are faithfully aligned head-to-tail along the individual molecular fibres.   In the case of the dimethoxide **2** the cyclodextrins of adjacent fibres are orientated in opposite directions (Figure 4 b)) and so the crystal is also non-polar and pseudo-centrosymmetric. Conversely, all the cyclodextrins of the rotaxanes **4**, including those in adjacent fibres, are aligned head-to-tail along a single axis (Figure 4 d)) and so the packing in the assembly is non-centrosymmetric and the crystal is polar.

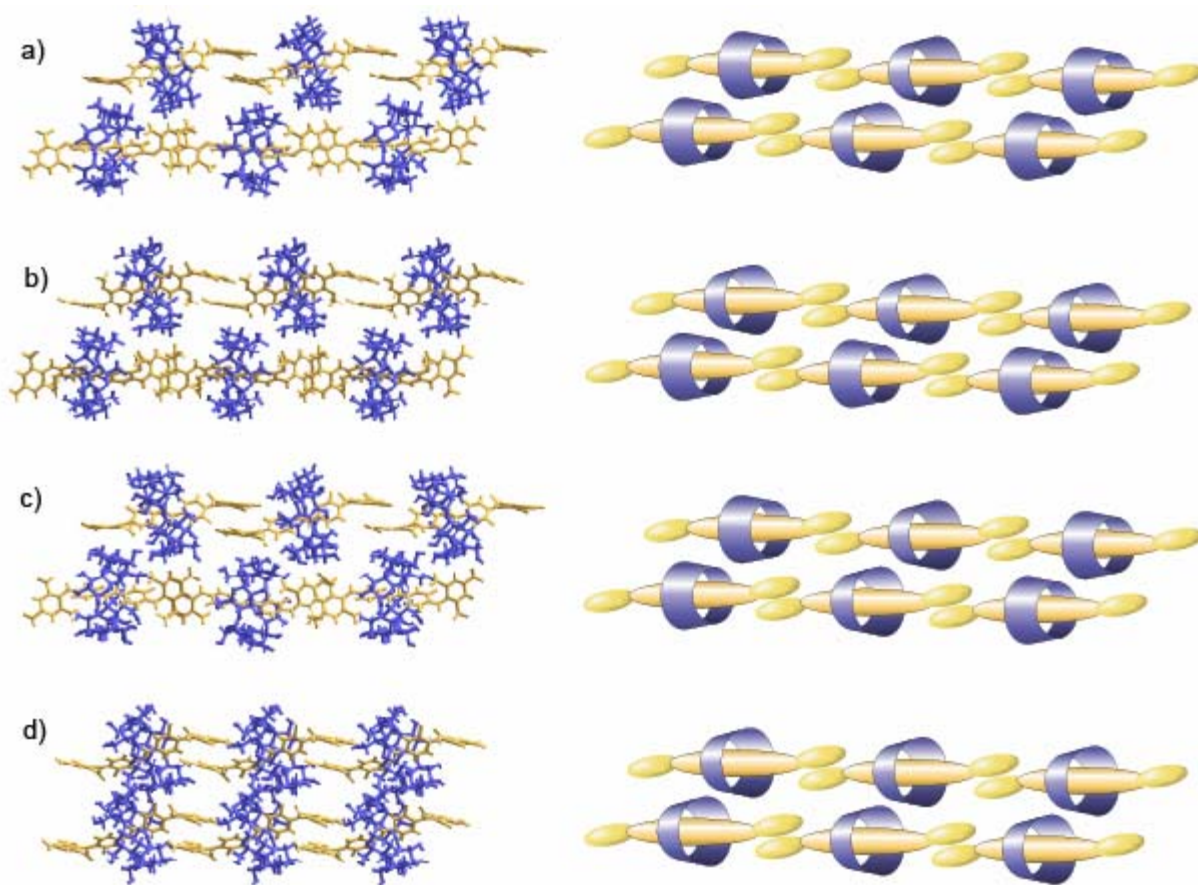Figure 4.   Crystal packing (left) and schematic representation of the alignment of the cyclodextrins (right) of two adjacent molecular fibres in a) the rotaxane **1**, b) the dimethoxide **2**, c) the difluoride **3** and d) the dichloride **4**.   In the truncated cone used to represent the cyclodextrins the wide (head) and narrow (tail) end correspond to the rims of secondary and primary hydroxyl groups respectively.

In conclusion ^{1}H NMR studies of the rotaxanes **1-4** have been used to establish that in each case the cyclodextrin is located around the stilbene moiety which rotates freely within the cyclodextrin annulus on the NMR time scale. The solid state assemblies of all four rotaxanes **1-4** show aligned molecular fibres of the dumbbells insulated by the cyclodextrins in which the interactions between the trinitrophenyl groups form a common structural motif. Interestingly, there were three different modes of alignment of the cyclodextrins in these fibres. While two of these represent centrosymmetric arrangements (for the rotaxanes **1-3**), the rotaxane **4** was found to form non-centrosymmetric and therefore polar crystals.

Experimental:

NMR spectra were recorded using either a Varian Mercury 300 spectrometer, operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C or a Varian Inova 500 spectrometer, operating at 500 MHz for ^{1}H and 125 MHz for [13]C. ROESY (mixing time of 200 to 280 ms) were obtained on the Inova 500 spectrometer and were referenced as described for [1]H. Methanol-d_4 with an isotopic purity of 99.8% and dimethyl sulfoxide-d_6 (DMSO-d_6) with an isotopic purity of 99.9% were purchased from Cambride Isotope Laboratories Inc., MA., and were referenced to $\delta = 3.31$ for ^{1}H and $\delta = 49.15$ for ^{13}C in Methanol-d_4 and $\delta = 2.50$ for ^{1}H and $\delta = 39.51$ for ^{13}C in DMSO-d_4.

Mass spectra were obtained using either VG Quattro II triple quadrupole MS instrument operating in either negative or positive modes for electrospray ionization mass spectrometry (ESI-MS) or a VG AutoSpec M series sector MS instrument for electron impact mass spectrometry (EI-MS). Elemental analyses were performed by the Australian National

University Microanalytical Services unit based at the Research School of Chemistry, Canberra, Australia. Melting points were measured on a Reichert hot-stage microscope apparatus and are uncorrected.

Thin layer chromatography (TLC) was performed on aluminium backed 0.2 mm thick silica gel 60 F254 plates as supplied by Merck. The running solvent was 5:4:3 (*n*-butanol:ethanol:water by volume). Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with an acidic naphthalene-1,3-diol (0.1% (weight to volume) of naphthalene-1,3-diol in solution of ethanol:water:H_2SO_4 (200:157:43, by volume)) followed by heating. The R_f values are reported relative to α-cyclodextrin. Flash chromatography was performed using analytical grade solvents and silica gel 60 (0.040-0.0063) as supplied by Merck. Semi-preparative high performance liquid chromatography (HPLC) was performed using a Waters Alliance Separation Module 2690 with a Waters 996 Photodiode array detector. Waters Millenium 3.2 operating system was used to control the instrument. Phenomenex Luna C_{18}, 250 x 10 mm column was used for the separations.

α-Cyclodextrin was obtained from Nihon Shokuhin Kako Co., Japan in 99.1% purity and was dried *in vacuo* over P_2O_5 to a constant weight. 2,4,6-Trinitrobenzene-1-sulfonic acid sodium salt dehydrate (TNBS) was purchased from Tokyo Kanei. Diaion HP-20 resin was purchased from Supelco, PA. 1-Fluoro-4-iodoaniline was obtained from Apollo Scientific Ltd. Other starting materials and reagents were obtained from Sigma-Aldrich, Merck or Lancaster Chemical companies and were used as supplied.

N-(2-Fluoro-4-iodophenyl)acetamide (6)

2-Fluoro-4-iodobenzenamine **5** (500 mg, 2.11 x 10^{-3} mol) was dissolved in DMF (5 cm^3). Acetic anhydride (2cm^3, 2.12 x 10^{-2} mol) was added and the mixture heated at 50 °C for 2 hours. The solution was cooled to room temperature and 1N HCl solution added (40 cm^3). EtOAc (4 x 50 cm^3) was used to extract the product from the aqueous solution. The organic layer was washed with water (3 x 40 cm^3) and dried using MgSO$_4$. The solvent was removed under reduced pressure to yield light purple solid of **6** (554 mg, 94%). ^{1}H NMR: (300 MHz, DMSO-d_6): δ 9.80 (1H, s, NH), 7.73 (1H, apparent t, *J* 8.4, ArH), 7.66 (1H, dd, *J* 10.2 and 1.8, ArH), 7.50 (1H, ddd, *J* 8.4, 1.8 and 0.9, ArH), 2.07 (3H, s, CH$_3$). ^{13}C NMR (125 MHz, DMSO-d_6): δ 168.8 (C=O), 153.1 (d, C-F), 133.2, 126.4 (C-NH), 125.4, 124.1, 87.0 (C-I), 23.5 (CH$_3$). EI-MS *m/z* % 279 (M$^{\bullet+}$, 70), 137 (100). Elemental analysis for C$_8$H$_7$FINO: Expected C 34.43, H 2.53, N 5.02; Found C 34.56, H 2.57, N 5.13.

(*E*)- 3,3'-Difluoro-4,4'-diacetamidestilbene (7) (Chris: not sure about this name)

Potassium fluoride (156 mg, 2.78 x 10^{-3} mol) and *n*-Bu$_4$NBr (578 mg, 1.79 x 10^{-3} mol) were suspended in toluene (5 cm^3) and *N*-(2-fluoro-4-iodophenyl)acetamide **6** (250 mg, 8.99 x 10^{-4} mol), Pd(OAc)$_2$ (20 mg, 8.91 x 10^{-5} mol) and vinyltrimethylsilane (1 cm^3, 6.82 x 10^{-3} mol) were added. The reaction was stirred vigorously at RT, under a nitrogen atmosphere for 40 hours. Wet DMF (4 cm^3) and PPh$_3$ (47 mg, 1.79 x 10^{-4} mol)) were added and the excess vinyltrimethylsilane removed under reduced pressure. After the addition of K$_2$CO$_3$ (310 mg, 2.24 x 10^{-3} mol) and a further equivalent of *N*-(2-fluoro-4-iodophenyl)acetamide **6** (250 mg, 8.99 x 10^{-4} mol) the stirring was continued at 85 °C for 24 hours. EtOAc (100 cm^3) was added to the cooled solution and the mixture filtered through Celite. The organic phase was washed with

water and brine (2 x 50 cm^3 each), dried with MgSO$_4$ and the solvent removed under reduced pressure. The product was purified by flash chromatography on silica gel or by HPLC to give a white solid of **7** (20 mg, 7%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.78 (2H, s, ArH), 7.93 (2H, apparent t, J 8.5, ArH), 7.50 (2H, dd, J 12.0 and 1.5, ArH), 7.33 (2H, apparent d, J 8.5, ArH), 7.20 (2H, s, olefinic), 2.11 (6H, s, CH$_3$). ^{13}C NMR (125 MHz, DMSO-d_6): δ 168.5 (C=O), 153.3 (d, C-F), 133.9, 127.2, 123.5 and 122.6, 125.5 (C-NH), 112.4, 23.4 (CH$_3$). ESI-MS (+ve) m/z (%) 353 (M+Na).

(E)-3,3'-Difluoro-4,4'-diaminostilbene (8)

(*E*)-3,3'-Difluoro-4,4'-diacetimidestilbene **7** (6 mg, 1.82 x 10^{-5} mol) was dissolved in ethanol (20 cm^3). Concentrated hydrochloric acid (5 cm^3) was added and the solution heated at reflux for 5 hours. The reaction was cooled, water added and the pH was made basic with sodium bicarbonate. The product was extracted with EtOAc (5 x 40 cm^3) and the solvent was evaporated to give an orange solid. The stilbene was subjected to HPLC giving a white product **8** (4 mg, 89%). ^{1}H NMR: (300 MHz, DMSO-d_6) δ$_H$ 7.23 (2H, d, J 12.9, ArH), 7.07 (2H, d, J 8.4, ArH), 6.85 (2H, s, ArH), 6.78 (2H, apparent t, J 8.4, ArH). ^{13}C NMR: (125 MHz, DMSO-d_6) δ$_C$ 151.2 (d, C-F), 134.3 (C-NH$_2$), 127.4 (C-CH), 124.8, 123.1 and 116.9, 112.1.

[(*E*)-4,4'-Bis(2,4,6-trinitrophenylamino)-3,3'-difluorostilbene]-[α-cyclodextrin]-[2]-rotaxane (3)

Stilbene **8** (3 mg, 1.22 x 10^{-5} mol) was equilibrated with α-cyclodextrin **12** (460 mg, 4.73 x 10^{-4} mol) in 0.2 M carbonate buffer (pH 10.0, 25 cm^3) at room temperature for 16 hours. Sodium TNBS **15** (10.5 mg, 2.99 x 10^{-5} mol) was added and the stirring continued for a further 4 hours. The reaction mixture was extracted with EtOAc (4 x 25 cm^3) and then the aqueous phase was concentrated to a volume of 50 cm^3. The solution was applied to a Diaion HP-20 column (250 x 15 mm). The column was washed with water until no unreacted α-cyclodextrin **12** was detected by TLC. A methanol/water gradient was applied. The fractions which contained the desired product (50-70% methanol) were combined and the solvent removed under reduced pressure. The crude product was dissolved in a small amount of water and purified by HPLC. After freeze drying, the title compound **3** was obtained as a red powder (4.5 mg, 73%). TLC: R_f 2.00. ^{1}H NMR (500 MHz, Methanol-d_4): δ 9.11 (2H, s, trinitrophenyl), 9.08 (2H, s, trinitrophenyl), 7.80 (1H, d, *J* 11.5, A-H5), 7.74 (1H, d, *J* 8.0, A-H4), 7.37 (1H, broad signals, A-H3), 7.29 (1H, apparent t, *J* 8.0, A-H9), 7.21-7.15 (3H, m, A-H10, H8 and H6), 7.07 (1H, d, *J* 16.5, A-H7), 4.95 (6H, d, *J* 3.5, CD-H1), 3.88 (6H, apparent t, *J* 9.5, CD-H3), 3.82-3.76 (12H, m, CD-H5 and H6), 3.67-3.59 (12H, m, CD-H4 and H6), 3.46 (6H, dd, J 10.0 and 3.5, A-H2). ^{13}C NMR (125 MHz, Methanol-d_4): δ 140.5, 140.1, 128.1, 127.9, 125.2, 125.5, 124.4, 116.1, 114.7 (stilbene and trinitrophenyl), 104.3 (CD-C1), 83.4 (CD-C4), 75.2 (CD-C3), 74.0 (CD-C2 and C5), 61.6 (CD-C6). ESI-MS (-ve) *m/z* (%) 1639 ((M-H), 100). HPLC: t_R 9.6 min (column: Phenomenex Luna, 250 x 10 mm; 26% aq. CH$_3$CN; flow rate: 2.5 cm^3 min^{-1}).

(*E*)-3,3'-Dichloro-4,4'-dinitrostilbene (10)

3-Chloro-4-nitrotoluene **9** (5 g, 2.91 x 10^{-2} mol) was dissolved in acetone (5 cm^3) and added dropwise to methanolic KOH (33%, by weight, 200 cm^3). Oxygen was bubbled through the

reaction mixture. The solution was stirred vigorously with ice bath cooling for 2 hours and then for a further 3 hours at RT. The solution was poured into 2 dm^3 of water. The resultant precipitate was collected by filtration and recrystallized three times from glacial acetic acid to give a yellow solid of **10** (1.86 g, 38%). M.p. 236-240 °C (lit.(REF9) 284-285 °C). δ_H (300 MHz, DMSO-d_6): 8.16 (2H, d, J 8.4, ArH), 8.04 (2H, d, J 1.5, ArH), 7.81 (2H, dd, J 8.4 and 1.5, ArH), 7.65 (2H, s, olefinic). EI-MS m/z (%) 338 (M$^{\bullet+}$, 100), 340 (63), 308 (35), 199 (50), 176 (75).

(*E*)-3,3'-Dichloro-4,4'-diaminostilbene (11)

(*E*)-3,3'-Dichloro-4,4'-dinitrostilbene **10** (200 mg, 5.8 x 10^{-4} mol) and SnCl$_2$.2H$_2$O (1.33g, 5.89 x 10^{-3} mol) were suspended in 8 cm^3 ethanol. The mixture was heated at 70 °C for 1 hour under nitrogen. The mixture was allowed to cool to room temperature and then poured onto ice. The pH was made basic (pH >8) by addition of sodium bicarbonate and then extracted with EtOAc (4 x 25 cm^3). The organic phase was dried using MgSO$_4$ and solvent evaporated under reduced pressure to give an orange solid of **11** (158 mg, 96%). ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.35 (2H, d, J 1.8, ArH), 7.20 (2H, dd, J 8.4 and 1.8, ArH), 6.81 (2H, s, olefinic), 6.75 (2H, d, J 8.4, ArH), 5.46 (4H, s, NH$_2$). ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.5 (C-NH$_2$), 126.8, 126.4, 125.4, 123.8, 117.2 and 115.3. EI-MS m/z (%) 278 (M$^{\bullet+}$, 100), 280 (75).

[(*E*)-4,4'-Bis(2,4,6-trinitrophenylamino)-3,3'-dichlorostilbene]-[α-cyclodextrin]-[2]-rotaxane (4)

α-Cyclodextrin **12** (2.5 g, 2.57 x 10^{-3} mol) was dissolved in 0.2 M carbonate buffer (pH 10.0, 25 cm^3). Stilbene **11** (100 mg, 3.58 x 10^{-4} mol) was added to the solution and left to equilibrate for 5 hours. The mixture was then sonicated for an hour before the addition of sodium TNBS **15** (278 mg, 7.92 x 10^{-4} mol). After 10 hours the solution was extracted with EtOAc (5 x 25 cm^3). The aqueous fraction was concentrated to about 10 cm^3 and water (40 cm^3) was added. The solution was applied to a Diaion HP-20 column (250 x 15 mm). The column was then washed with water until no unreacted α-cyclodextrin **12** was detected by TLC and then eluted with increasing amount of methanol. The fractions containing the desired product (50-70% Methanol) were combined and the solvent evaporated. The solid was dissolved in 1 cm^3 of water and subjected to HPLC. The desired fraction was collected and freeze dried to give product **4** as a red powder (9 mg, 2%). TLC: R_f 2.05 (relative to α-cyclodextrin). M.p. 264-270 °C (dec.). ^{1}H NMR (500 MHz, Methanol-d_4): δ 9.10 (4H, broad, trinitrophenyl), 8.05 (1H, s, A-H5), 7.85 (1H, d, *J* 8.0, A-H4), 7.36 (1H, s, A-H8), 7.29 (2H, m, A-H3 and H10), 7.21 (1H, m, A-H9), 7.13 (1H, d, *J* 16.5, A-H6), 7.04 (1H, d, *J* 16.5, A-H7), 4.95 (6H, d, *J* 3.0, CD-H1), 3.89 (6H, apparent t, *J* 9.0, CD-H3), 3.82-3.77 (12H, m, CD-H5 and H6), 3.67-3.61 (12H, m, CD-H4 and H6), 4.46 (6H, dd, *J* 3.0 and 9.5, CD-H2). ^{13}C NMR (75 MHz, Methanol-d_4): δ 140.5, 139.9, 130.7, 130.5, 130.1, 130.0, 129.1, 128.7, 128.2, 128.2, 127.7, 126.5, 124.4, 123.7 (stilbene and trinitrophenyl), 104.3 (CD-C1), 83.4 (CD-C4), 75.2 (CD-C3), 74.1 and 74.0 (CD-C2 and C5), 61.6 (CD-C6). ESI-MS (-ve) *m/z* (%) 1671 (M-H, 90), 1673 (100). Elemental analysis for $C_{62}H_{74}Cl_2N_8O_{42}$.$9H_2O$:

Expected C 40.55, H 5.05, N6.10; Found C 40.71, H 4.79, N5.74. HPLC: t_R 19.7 min (column: Phenomenex Luna, 250 x 10 mm; 22% aq. CH$_3$CN; flow rate: 2.5 cm^3 min^{-1}).

X-Ray Crystallography

The crystal data, data collection and refinement parameters are listed below. Measurements were made with a Nonius KappaCCD area detector using Mo Kα (λ = 0.71073 Å) radiation. The intensities were corrected for Lorentz and polarisation effects and for absorption. The structures were solved by direct methods using SHELXM (REF13) and refined on F^2 using all data by full-matrix least-squares procedures using SHELXL-97 (REF14). All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in calculated positions except for the many water molecules in each structure which were included only as oxygen atoms. In the structure of **3**, the orientations of two of the hydroxymethyl groups of one of the independent cyclodextrin units were disordered over two positions, as well as disorder in the position of one of the fluorine atoms.

Crystallographic data, as CIF files, have been deposited with the Cambridge Crystallographic Data Centre (CCDC No 295511 and 295512). Copies can be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (e-mail: deposit@ccdc.cam.ac.uk).

Crystal data for **3**: C$_{62}$H$_{74}$F$_2$N$_8$O$_{54}$, *M* = 1833.3, monoclinic, *a* = 13.4409(4), *b* = 17.3928(5), *c* = 34.6908(10) Å, β = 94.2146(7)°, *V* = 8087.9(4) Å^3, F(000) = 3808, *T* = 200 K, space group *P*2$_1$, *Z* = 4, orange plate, 0.40 x 0.36 x 0.08 mm^3, μ = 0.137 mm^{-1}, D$_c$ = 1.506 g.cm^{-3}, 116052 reflections measured, 28053 unique [R_{int} = 0.0651], 2325 parameters, *wR*$_2$ (all data) = 0.2032, *R*$_1$ [24339 data with I>2σ(I)] = 0.0754.

Crystal data for **4**: $C_{62}H_{74}Cl_2N_8O_{52.5}$, *M* = 1842.2, monoclinic, *a* = 17.7801(1), *b* = 16.2393(1), *c* = 27.3531(2) Å, β = 94.2746(4)°, *V* = 7875.9(1) Å^3, F(000) = 3824, *T* = 200 K, space group $P2_1$, *Z* = 4, red prism, 0.26 x 0.24 x 0.22 mm^3, μ = 0.202 mm^{-1}, D_c = 1.554 g.cm^{-3}, 201686 reflections measured, 35994 unique [R_{int} = 0.0450], 2251 parameters, wR_2 (all data) = 0.1810, R_1 [28985 data with I>2σ(I)] = 0.0630.

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