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Hydrogen bond templated synthesis of catenanes and rotaxanes from a single isophthalic acid derivative†

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Hydrogen bond templated [2]catenanes and [2]rotaxanes have been synthesized using azide precursors derived from a single isophthalic acid derivative precursor. The interlocked molecules were prepared using either stoichiometric or near stoichiometric amounts of macrocycle and CuAAC "click" precursors, with yields of up to 70% for the mechanical bond formation step. Successful preparation of the interlocked structures was confirmed by NMR spectroscopy and mass spectrometry, with detail of co-conformational behaviour being elucidated by a range of ^{1}H NMR spectroscopic experiments.

Introduction

Mechanically interlocked molecules such as catenanes[1] (consisting of interlocked macrocyclic rings) and rotaxanes[2] (macrocyclic rings(s) trapped on stoppered axles) have unusual properties arising from the mechanical bond such as the potential for the controlled, large amplitude motion of the interlocked components and the 3D cavities and spaces arising from their exotic architectures.[3]

An array of template methodologies have been used to prepare interlocked molecules, including but not limited to, metal cations,[4] π–π stacking (or π-donor/π-acceptor interactions),[5] hydrogen bonding[6] and anions.[7] However, the bespoke nature of many syntheses of catenanes and rotaxanes is often a drawback when trying to exploit their properties and potential applications. Development of modular methodologies based on easy to access building blocks is desirable.

While our group has reported upon the rapid hydrogen bond templated synthesis of [2]rotaxanes in good yield,[8,9] our previous serendipitous [2]catenane synthesis is low yielding (12%) with regard to the crucial covalent capture step that forms the interlocked compound.[10,11] We hypothesized that with design modification to allow for more efficient hydrogen bonding templation, that synthesis of [2]catenanes in higher yields should be possible.

Indeed, here in we report the successful synthesis of three novel [2]catenanes derived from a simple isophthalic acid precursor in good yield. Furthermore, starting from the same isophthalic acid derivative allowed for the synthesis of two novel [2]rotaxanes in reasonable yield. All interlocked molecules were characterized by NMR and IR spectroscopy and mass spectrometry.

Results and discussion

Synthesis and characterization of catenanes

The catenane syntheses all build upon azido-functionalized isophthalic acid derivative **1** (Scheme 1), which may be rapidly prepared from commercially available mono-methyl ester of isophthalic acid.[12,13]

Three azide–alkyne coupling partners were prepared. Initially DCC/*N*-hydroxysuccinimide-mediated amide coupling of alkyne carboxylic acids **2–4** [14–16] with commercially available 4-(Boc-amino)benzylamine afforded alkynes **5–7**. These were subsequently deprotected using TFA, with removal of the Boc group in quantitative yield confirmed by ^{1}H NMR spectroscopy.

The alkyne–azide precursor targets **11–13** were synthesized *via* the coupling of the amine trifluoroacetate salts **8–10** with isophthalic acid derivative **1** using DCC and *N*-hydroxysuccinimide. Following workup and purification by silica gel column chromatography, **11–13** were isolated in reasonable yields (51–64%). The successful preparation of novel compounds **11–13** was confirmed by NMR spectroscopy and mass spectrometry (see ESI, pp. S9 and S10; S14 and S15; S19 and S20†).

Mechanical bond formation was accomplished *via* the threading and cyclization of alkyne-azides **11–13** through previously reported macrocycle **14**.[10] In each case, to a solution of **14** in dry CH_2Cl_2, 1.0 equivalents of **11–13** was added and allowed to stir for 15 minutes to facilitate pseudorotaxane for-

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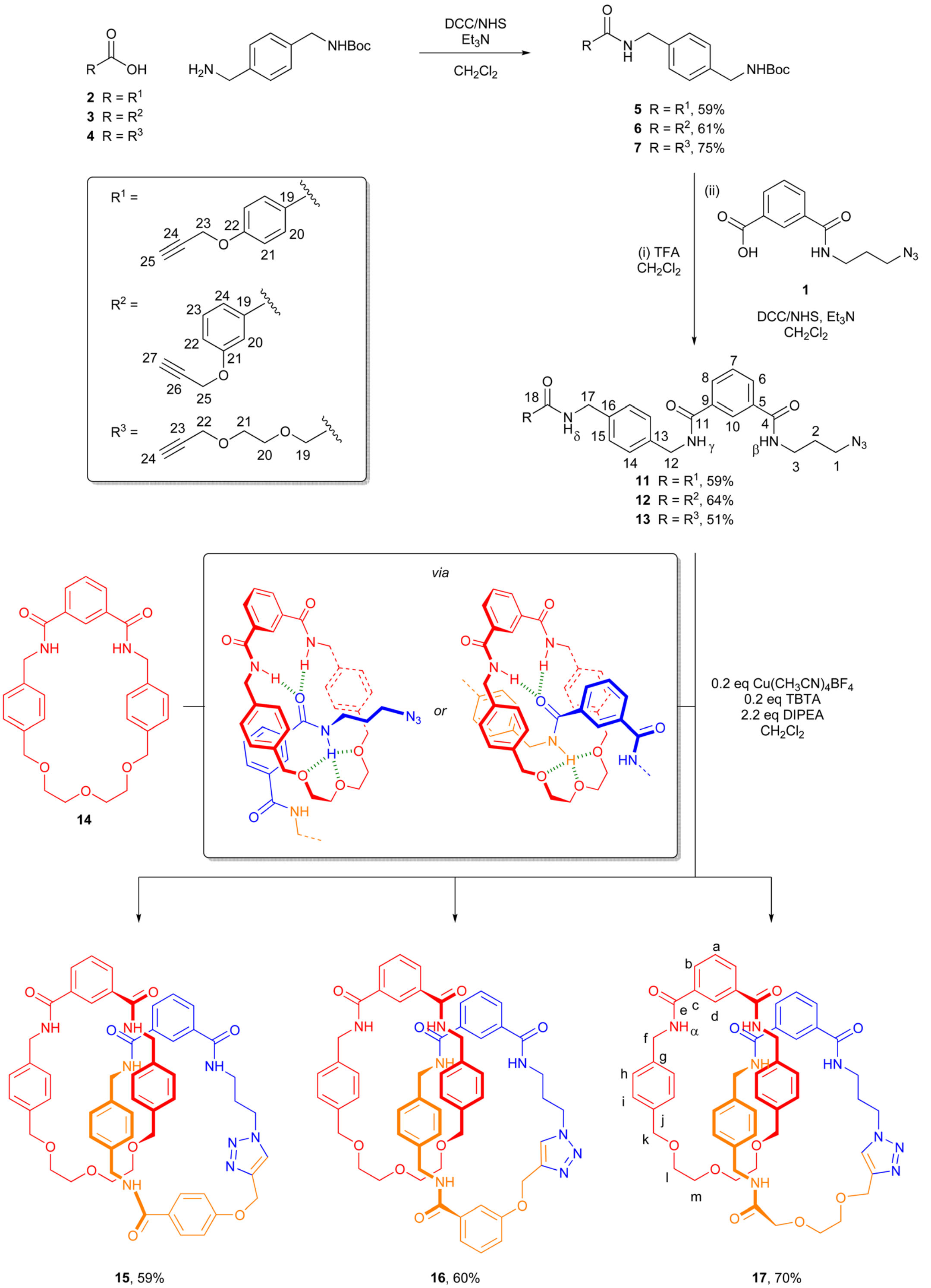


Scheme 1 Synthesis of [2]catenanes **15–17**.

mation (Scheme 1). Then, catalytic $Cu(CH_3CN)_4BF_4$ and TBTA (tris((1-benzyl-4-triazolyl)methyl)amine), and 1.2 equivalents of *N*,*N*-diisopropylamine were added. The reactions were stirred overnight at room temperature under an inert atmosphere, and then submitted to aqueous workup and purification by silica gel column chromatography. Novel heterocircuit [2]catenanes **15–17**[17,18] were isolated in good yields (59–70%). The [2]catenanes were characterized by ^1H & ^{13}C NMR and IR spectroscopy, with molecular ions being detected by high resolution mass spectrometry (see ESI, pp. S21–S26†).

Catenane formation is evident upon comparison of the ^1H NMR spectra of precursor **13**, macrocycle **14** and [2]catenane

17 (Fig. 1). The upfield shift and splitting of aromatic protons *14*/*15* and *h*/*i* in catenane **17** compared to **13** and **14** is consistent with the intercalation of aromatic rings within the interlocked structure. The downfield shift of internal isophthalamide proton *d* is indicative of interactions with a hydrogen bond acceptor on the cyclized thread. Another notable characteristic of the ^{1}H NMR spectra of catenanes **15–17** is the splitting of certain protons (*e.g. f* and *k*) due to the two faces of the rotationally symmetric macrocycle becoming inequivalent due to the directionality of the newly formed rotationally asymmetric macrocyclic ring.

Further evidence of the interlocked nature of the macrocyclic rings is provided by a molecular ion peak being identifiable by positive ion electrospray mass spectrometry (see ESI, pp. S22, S24 & S26†). In addition, for each catenane there is the appearance of multiple through-space correlations in the ^{1}H–^{1}H ROESY NMR spectra between resonances arising from protons in the two interlocked macrocycles (*e.g.* Fig. 2 and see ESI, pp. S39–S41†). Inspection of the entire spectrum in each case reveals sufficient intercomponent correlations to indicate the macrocyclic rings of the catenane are switching between multiple co-conformations in 1 : 1 $CDCl_3/CD_3OD$ (see ESI, p. S42†).

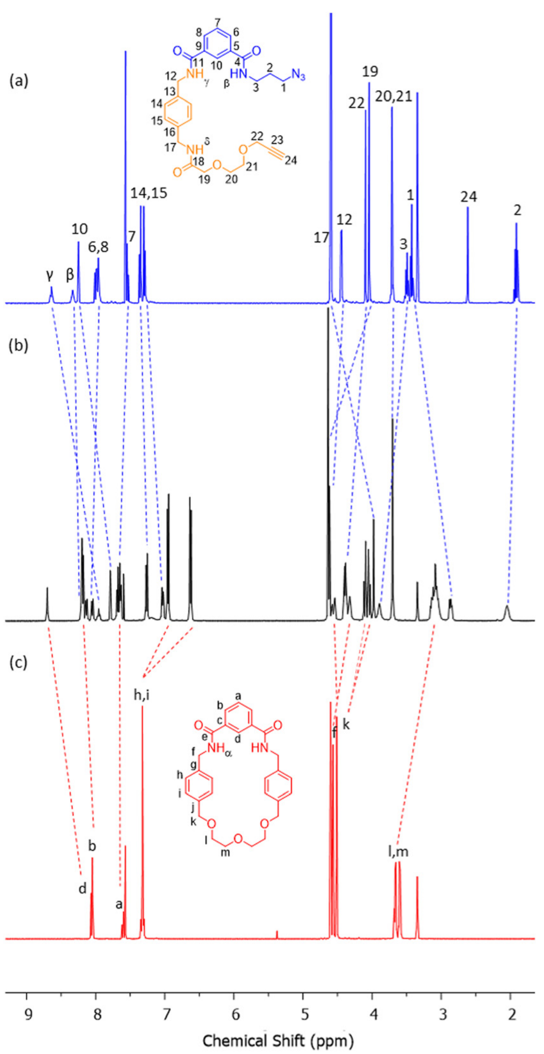


Fig. 1 ^{1}H NMR spectra of (a) alkyne–azide **13**, (b) [2]catenane **17** and (c) macrocycle **14** (1 : 1 $CDCl_3/CD_3OD$, 400 MHz, 298 K).

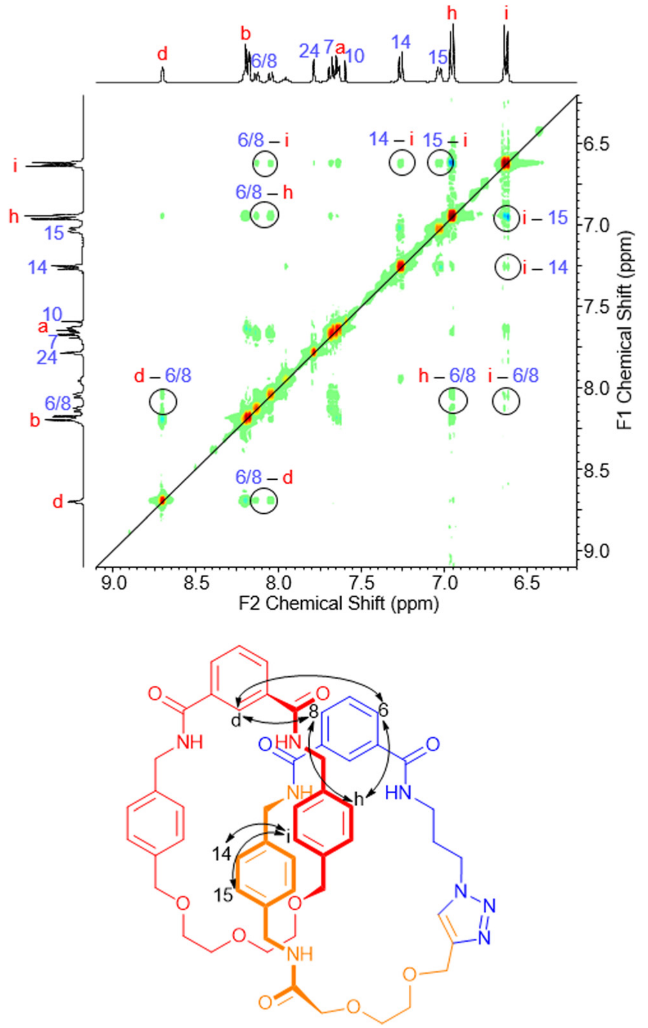


Fig. 2 Section of ^{1}H–^{1}H ROESY NMR spectrum of [2]catenane **17** with intercomponent through-space correlations highlighted (1 : 1 $CDCl_3/CD_3OD$, 400 MHz, 298 K).

To probe potential dynamic interactions (*e.g.* the pirouetting of the interlocked macrocyclic rings) the most soluble [2] catenane, glycol catenane **17**, was studied by variable temperature (VT) ^{1}H NMR spectroscopy in $C_2D_2Cl_4$ (Fig. 3). At (and below) room temperature, several C–H resonances are broad, but these sharpen upon heating. Three of the amide N–H resonances not only sharpen but move upfield, while one (δ) has almost no change in chemical shift, indicating that this amide N–H is participating in intramolecular hydrogen bonding.

Synthesis and characterization of rotaxanes

The azido-functionalized isophthalic acid derivative **1** can also be derivatized with bulky stopper groups to allow for the formation of rotaxanes (Scheme 2). Novel half-axle components

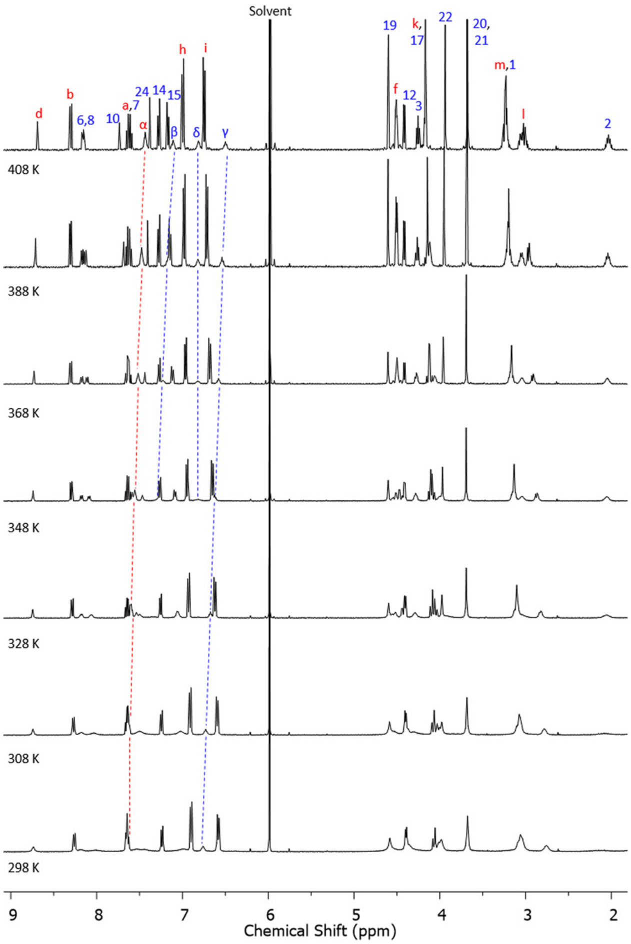


Fig. 3 ^{1}H NMR spectra of [2]catenane **17** recorded at T = 298 K to 408 K in $C_2D_2Cl_4$ (400 MHz). See Scheme 1 or Fig. 1 for atom labels.

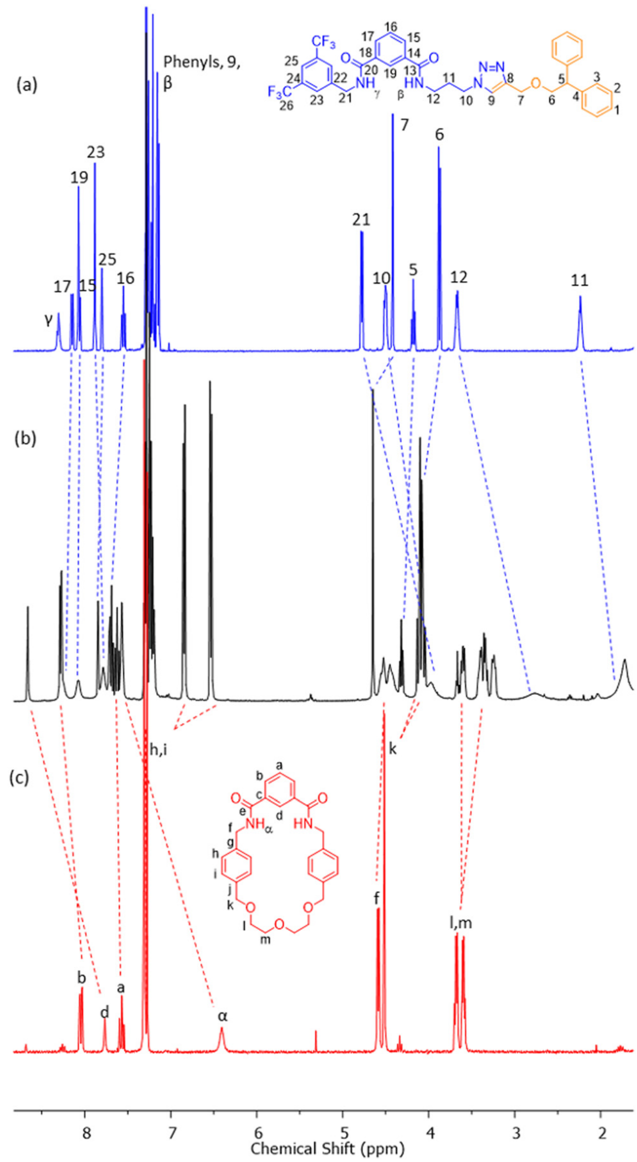
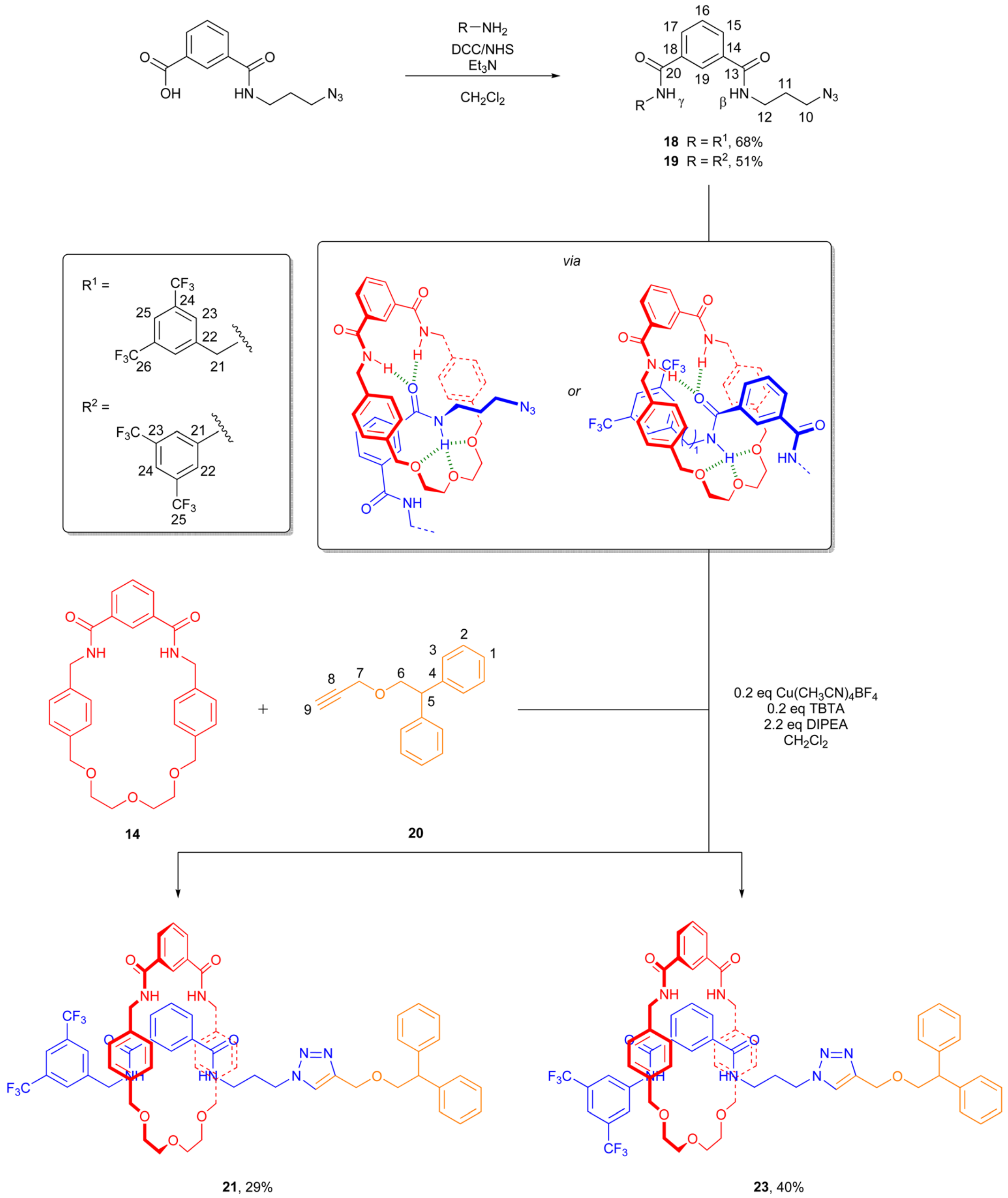


Fig. 4 ^{1}H NMR spectra of (a) axle **22**, (b) [2]rotaxane **21** and (c) macrocycle **14** ($CDCl_3$, 400 MHz, 298 K).

18 and **19** were prepared in good yield by reaction of 3,5-bis(trifluoromethyl)benzylamine and 3,5-bis(trifluoromethyl)-aniline with isophthalic acid derivative **1** activated using DCC and *N*-hydroxysuccinimide.

To prepare [2]rotaxanes **21** and **23**, 1.1 equivalents of **18** or **19** and alkyne **20** [8] were added to a solution of macrocycle **14** in dry CH_2Cl_2, followed by catalytic $Cu(CH_3CN)_4BF_4$ and TBTA, and 1.2 equivalents of *N*,*N*-diisopropylamine. Following aqueous workup and purification of the crude material by preparative TLC, [2]rotaxanes **21** and **23** were isolated in 29% and 40% yields respectively.[19] While the isolated yields are reasonable, it should be noted the actual yields of rotaxane formation are almost certainly higher. Isolation of pure rotaxane was hindered in both cases by incomplete separation of product bands during chromatographic purification.

Successful formation of the [2]rotaxanes was confirmed by analysis of NMR spectra and detection of molecular ion peaks in high resolution mass spectrometry (see ESI, pp. S31–S34†). The ^{1}H NMR spectrum of rotaxane **21**, along with that of non-interlocked macrocycle **14** and axle **22** for comparison, is shown in Fig. 4. Once again, the upfield shift and splitting of aromatic protons *h* and *i* in the interlocked molecule compared to non-interlocked macrocycle **14** is consistent with presence of the second component (here an axle) between the aromatic rings of the macrocycle. The downfield shift of proton *d* and the amide protons *α* of the macrocycle in the rotaxane are indicative of interactions with a hydrogen bond acceptor on the axle. In the ^{1}H–^{1}H ROESY NMR spectra of both rotaxanes there are through-space correlations between resonances arising from protons in the two interlocked components (see ESI, pp. S43 & S44†). For rotaxane **21**, the multiple observed intercomponent correlations strongly support the primary location of the macrocyclic ring component as being in the vicinity of the axle isophthalamide in $CDCl_3$ (see ESI, p. S45†). Meanwhile for rotaxane **23** there is evidence the macrocyclic ring preferentially resides over the isophthalamide amide N–



Scheme 2 Synthesis of [2]rotaxanes **21** and **23**.

Hγ due to the observable correlations being between stopper proton *22* and ring protons *i* and *l* (see ESI, p. S45†).

Conclusions

Using precursors prepared from isophthalic acid derivative **1**, we have demonstrated the hydrogen bond templated synthesis of both [2]catenanes and [2]rotaxanes. Despite using only stoichiometric (or near stoichiometric) quantities of precursors, yields of up to 70% for the crucial covalent capture step are possible. This work demonstrates synthetic methodologies that have the potential to incorporate a range of functionality into either the ring of a catenane or the stoppers of a rotaxane in a modular approach in good yields. Investigations into deploying these methodologies, including preparing mechanically chiral analogues,[20] are ongoing in our laboratories.

Experimental

General information

All reagents and solvents were used as obtained from commercial suppliers, unless otherwise stated. Dry solvents, Et_3N and DIPEA were purchased dry and stored under an inert atmosphere. $Cu(CH_3CN)_4BF_4$ was stored in a desiccator over P_4O_{10}.

Petrol refers to the fractions of petroleum that boil between 40 °C and 60 °C. Deionized water was used in all cases. All aqueous solutions are saturated unless otherwise stated.

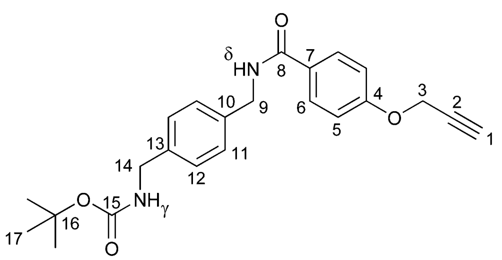
Azido-functionalized isophthalic acid derivative **1**,[12] alkyne benzoic acids **2**[14] and **3**,[15] alkyne ethylene glycol acid **4**,[16] macrocycle **14**,[9,10] alkyne **20**[8] were all synthesized based on previously reported procedures.

Silica gel with a 60 Å particle size was used as the stationary phase for column chromatography. Analytical TLC was used to monitor the progress of column chromatography, with TLC plates examined under short wavelength (254 nm) UV light, or staining with potassium permanganate and phosphomolybdic acid solutions as appropriate. Preparatory TLC was carried out on silica gel possessing a fluorescent indicator to allow for examination with short wavelength UV light.

IR spectra were recorded on an Agilent Technologies Cary 630 FTIR spectrometer. NMR spectra were recorded on a Bruker AVANCE III 400 or a Bruker Fourier 300 spectrometer at 298 K (unless otherwise stated). Mass spectra were recorded on a Shimadzu LCMS IT ToF instrument. Melting points were recorded on a Gallenkamp capillary melting point apparatus and are uncorrected.

Experimental procedures

Alkyne 5. To a solution of **2** (200 mg, 1.14 mmol) dissolved in dry CH_3CN (10 mL) was added DCC (281 mg, 1.36 mmol) and *N*-hydroxysuccinimide (157 mg, 1.36 mmol). The solution was stirred at room temperature under nitrogen for 16 hours. The solution was then filtered under gravity and the solvent removed *in vacuo* to afford an off-white solid. The crude material was redissolved in dry CH_2Cl_2 (20 mL) and 4-(Boc-amino)benzylamine (268 mg, 1.14 mmol) was added to the solution followed by dry Et_3N (0.19 mL, 1.36 mmol). The solution was stirred at room temperature under nitrogen for 16 hours. The mixture was then washed with aq. 1 M HCl (2 × 20 mL), aq. $NaHCO_3$ (2 × 20 mL) and water (1 × 20 mL). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to afford an off-white solid. Purification by flash column chromatography (EtOAc : petrol 2 : 1) gave the *title product* (262 mg, 59%) as a colourless solid.



R_f 0.60 (EtOAc : petrol 2 : 1).

m.p. 84–85 °C.

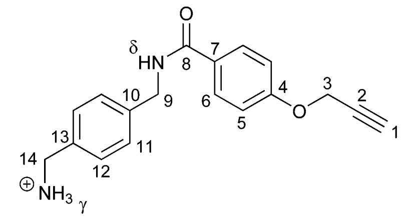
ν_{max}/cm^{-1} **(neat):** 3315 (N–H), 3274 (N–H), 2928 (C–H), 1677 (C═O), 1632 (C═O).

δ_H **(400 MHz, $CDCl_3$):** 7.77 (2H, d, J = 9.0 Hz, H^5), 7.34–7.20 (4H, m, H^{11} & H^{12}), 7.01 (2H, d, J = 9.0 Hz, H^6), 6.28 (1H, bs, NH^δ), 4.83 (1H, bs, NH^γ), 4.75 (2H, d, J = 2.4 Hz, H^3), 4.63 (2H, d, J = 5.7 Hz, H^9), 4.31 (2H, d, J = 6.1 Hz, H^{14}), 2.54 (1H, t, J = 2.4 Hz, H^1), 1.47 (9H, s, H^{17}).

δ_C **(100 MHz, $CDCl_3$):** 166.6 (C^8) 166.5 (C^{15}), 160.0 (C^4), 138.4 (C^7), 137.4 (C^{10}), 128.7 (C^6), 128.2 (C^{12}), 127.8 (C^{11}), 127.4 (C^{13}), 114.6 (C^5), 79.5 (C^2), 79.1 (C^{16}), 76.0 (C^1), 55.6 (C^3), 44.3 (C^{14}), 43.7 (C^9), 28.3 (C^{17}).

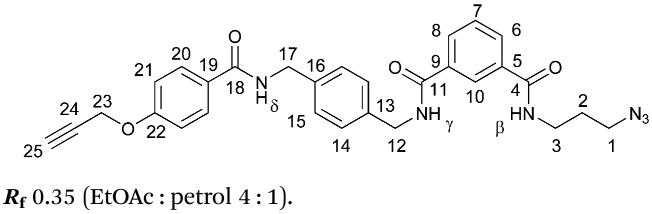
m/z **(ESI):** 417.1785 ($[M + Na]^+$ $C_{23}H_{26}N_2NaO_4$ requires 417.1769).

Deprotected amine–alkyne salt 8. To a solution of Boc-alkyne **5** (255 mg, 0.65 mmol) in CH_2Cl_2 (5 mL) cooled to 0 °C was added trifluoroacetic acid (1 mL, 3.7 mmol). The solution was warmed to room temperature and stirred for 2 hours, then the volatiles were removed *in vacuo*. The product was isolated as the TFA salt. Boc deprotection was confirmed by ^1H NMR analysis and the material was taken forward immediately without further purification.



δ_H **(300 MHz, D_6-DMSO):** δ 8.96 (1H, t, J = 6.0 Hz, NH^δ), 8.28–7.96 (3H, m, NH_3^+), 7.90–7.82 (2H, m, H^5), 7.42–7.30 (4H, m, H^{12} & H^{11}), 7.08–7.02 (2H, m, H^6), 4.87 (2H, d, J = 2.4 Hz, H^3), 4.46 (2H, d, J = 6.0 Hz, H^9), 4.00 (2H, q, J = 5.6 Hz, H^{14}), 3.60 (1H, t, J = 2.4 Hz, H^1).

Alkyne–azide 11. To a solution of **1** (62 mg, 0.25 mmol) dissolved in dry CH_3CN (5 mL) was added DCC (61 mg, 0.32 mmol) and *N*-hydroxysuccinimide (31 mg, 0.29 mmol). The reaction was then stirred at room temperature under nitrogen for 16 hours. The resulting suspension was filtered under gravity and the solvent removed *in vacuo* to afford a white solid. The crude material was then redissolved in dry CH_2Cl_2 (20 mL) and **8** (102 mg, 0.25 mmol) and dry Et_3N (0.10 mL, 0.72 mmol) were added. The solution was then stirred at room temperature under nitrogen for 16 hours. The mixture was then washed with aq. 1 M HCl (2 × 20 mL), aq. $NaHCO_3$ (2 × 20 mL) and water (1 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo* to afford a colourless solid. Purification by flash column chromatography (EtOAc : petrol 3 : 1–4 : 1) gave the *title product* (77 mg, 59%) as a colourless solid.



R_f 0.35 (EtOAc : petrol 4 : 1).

m.p. 120–122 °C.

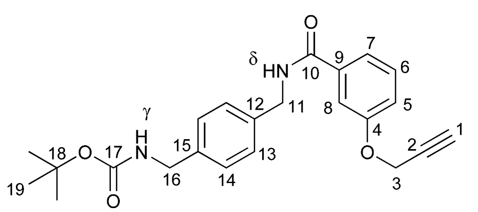
ν_{max}/cm^{-1} **(neat):** 3281 (C≡C–H), 2929 (C–H), 2102 (N=N=N), 1621 (C=O), 1541 (C–N).

δ_H **(400 MHz, 9 : 1 $CDCl_3/CD_3OD$):** 8.17 (1H, bs, H^{10}), 7.94 (1H, d, J = 9.0 Hz, $H^{6/8}$) 7.90 (1H, d, J = 9.0 Hz, $H^{6/8}$), 7.74 (2H, d, J = 8.9 Hz, H^{21}), 7.44 (1H, app. t, H^7), 7.20–7.10 (4H, m, H^{14} & H^{15}), 6.94 (2H, d, J = 8.9 Hz, H^{20}), 4.69 (2H, d, J = 2.4 Hz, H^{23}), 4.48 (2H, d, J = 6.0 Hz, H^{17}), 4.43 (2H, d, J = 5.7 Hz, H^{12}), 3.39–3.35 (2H, m, H^3), 3.30 (2H, t, J = 9.0 Hz, H^1), 2.55 (1H, t, J = 2.4 Hz, H^{25}), 1.78 (2H, quintet, J = 6.5 Hz, H^2).

δ_c **(100 MHz, 9 : 1 $CDCl_3/CD_3OD$):** 167.6 (C^{11}), 167.4 (C^{18}), 167.2 (C^4), 160.1 (C^{22}), 137.6 (C^{13}), 137.1 ($C^{5/9/19}$) 137.0 (C^{16}), 134.3 ($C^{5/9/19}$), 134.2 ($C^{5/9/19}$), 130.4 ($C^{6/8}$), 130.4 ($C^{6/8}$) 129.1 (C^{21}), 129.0 (C^7), 127.9 (C^{15}), 127.0 (C^{14}), 125.2 (C^{10}), 114.6 (C^{20}), 77.8 (C^{24}), 76.0 (C^{25}), 55.7 (C^{23}), 49.1 (C^1), 43.7 (C^{17}), 43.4 (C^{12}), 37.4 (C^3), 28.5 (C^2).

m/z **(ESI):** 525.2245 ($[M + H]^+$ $C_{29}H_{29}N_6O_4$ requires 525.2231).

Alkyne 6. To a solution of **3** (224 mg, 1.27 mmol) dissolved in dry CH_3CN (10 mL) was added DCC (314 mg, 1.35 mmol) and *N*-hydroxysuccinimide (175 mg, 1.27 mmol). The solution was stirred at room temperature under nitrogen for 16 hours. The solution was then filtered under gravity and the solvent removed *in vacuo* to afford an off-white solid. The crude material was redissolved in dry CH_2Cl_2 (20 mL) and 4-(Boc-amino)benzylamine (300 mg, 1.27 mmol) was added to the solution followed by dry Et_3N (0.22 mL, 1.67 mmol). The solution was stirred at room temperature under nitrogen for 16 hours. The mixture was then washed with aq. 1 M HCl (2 × 20 mL), aq. $NaHCO_3$ (2 × 20 mL) and water (1 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo* to afford an off-white solid. Purification by flash column chromatography (EtOAc : Hexane 2 : 3–1 : 1) gave the *title product* (306 mg, 61%) as a colourless solid.



R_f 0.87 (EtOAc : petrol 1 : 2).

m.p. 118–120 °C.

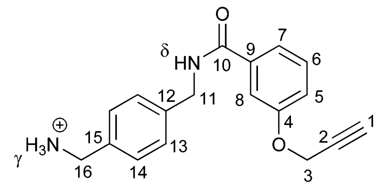
ν_{max}/cm^{-1} **(neat):** 3310 (C≡C–H), 3270 (N–H), 2930 (C–H), 1672 (C=O), 1635 (C=O).

δ_H **(400 MHz, $CDCl_3$):** 7.48–7.45 (1H, m, H^8), 7.38–7.29 (6H, m, H^{14}, H^{13}, H^5 & H^7), 7.16–7.11 (1H, m, H^6), 6.38 (1H, bs, NH^{δ}), 4.88 (1H, bs, NH^{γ}), 4.75 (2H, d, J = 2.4 Hz, H^3), 4.64 (2H, d, J = 5.8 Hz, H^{11}), 4.32 (2H, d, J = 5.8 Hz, H^{16}), 2.55 (1H, t, J = 2.4 Hz, H^1), 1.48 (9H, s, H^{19}).

δ_C **(100 MHz, $CDCl_3$):** 166.9 (C^{10}) 166.8 (C^{17}), 157.8 (C^4), 138.5 (C^{12}), 137.1 (C^{15}), 135.9 (C^{13}), 129.7 (C^6), 128.2 (C^{14}), 127.8 (C^{19}), 119.6 (C^5), 118.5 (C^7), 113.5 (C^8), 79.1 (C^{18}), 78.0 (C^2), 75.9 (C^1), 55.9 (C^3), 44.3 (C^{11}), 43.8 (C^{16}), 28.4 (C^{19}).

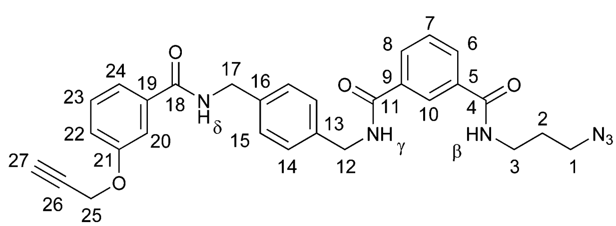
m/z **(ESI):** 417.1785 ($[M + Na]^+$ $C_{23}H_{26}N_2NaO_4$ requires 417.1771).

Deprotected amine-alkyne salt 9. To a solution of Boc-alkyne **6** (299 mg, 0.76 mmol) in CH_2Cl_2 (5 mL) cooled to 0 °C was added trifluoroacetic acid (1 mL, 3.7 mmol). The solution was warmed to room temperature and stirred for 2 hours, then volatiles were removed *in vacuo*. The product was isolated as the TFA salt. Boc deprotection was confirmed by ^1H NMR analysis and the material was taken forward immediately without further purification.



δ_H **(400 MHz, D_6-DMSO):** 9.06 (1H, t, J = 6.0 Hz, NH^{δ}), 8.28–7.96 (3H, m, NH_3^+), 7.54–7.47 (2H, m, H^5 & H^7), 7.44–7.34 (5H, m, H^8, H^{14} & H^{13}), 7.19–7.14 (2H, m, H^6), 4.86 (2H, d, J = 2.3 Hz, H^3), 4.48 (2H, d, J = 6.0 Hz, H^{11}), 4.02 (2H, q, J = 5.8 Hz, H^{16}), 3.60 (1H, t, J = 2.4 Hz, H^1).

Alkyne–azide 12. To a solution of **1** (182 mg, 0.73 mmol) dissolved in dry CH_3CN (10 mL) was added DCC (185 mg, 0.90 mmol) and *N*-hydroxysuccinimide (103 mg, 0.90 mmol). The reaction was stirred at room temperature under nitrogen for 16 hours. The resulting suspension was filtered under gravity and the solvent removed *in vacuo* to afford a white solid. The crude material was then redissolved in dry CH_2Cl_2 (20 mL) and **9** (220 mg, 0.75 mmol) and dry Et_3N (0.26 mL, 2.00 mmol) were added. The solution was stirred at room temperature under nitrogen for 16 hours. The mixture was then washed with aq. 1 M HCl (2 × 20 mL), aq. $NaHCO_3$ (2 × 20 mL) and water (1 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo* to afford a colourless solid. Purification by flash column chromatography (EtOAc : petrol 5 : 1) gave the *title product* (253 mg, 64%) as a colourless solid.



R_f = 0.23 (EtOAc : petrol 3 : 1).

m.p. 122–124 °C.

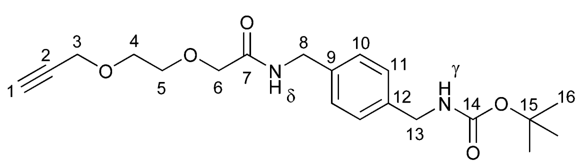
ν_{max}/cm^{-1} **(neat):** 3291 (N–H), 2926 (C–H), 2098 (N=N=N), 1634 (C=O), 1533 (C–N).

δ_H **(400 MHz, $CDCl_3$):** 8.36 (1H, s, H^{10}), 8.08 (1H, d, J = 7.7 Hz, $H^{6/8}$), 7.98 (1H, d, J = 7.7 Hz, $H^{6/8}$), 7.53–7.48 (1H, m, H^7), 7.49–7.47 (1H, m, H^{20}), 7.46–7.43 (1H, m, $H^{24/22}$), 7.35 (1H, t, J = 7.7 Hz, H^{23}), 7.21–7.13 (4H, m, $H^{22/24}$ & $NH^{\beta,\ \gamma,\ \delta}$), 7.10 (2H, d, J = 8.9 Hz, H^{15}), 7.01 (2H, d, J = 8.9 Hz, H^{14}), 4.71 (2H, d, J = 2.4 Hz, H^{25}), 4.51 (2H, d, J = 5.8 Hz, H^{17}), 4.36 (2H, d, J = 5.8 Hz, H^{12}), 3.32 (2H, q, J = 6.6 Hz, H^{3}), 3.25 (2H, t, J = 6.6 Hz, H^{1}), 2.53 (1H, t, J = 2.4 Hz, H^{27}), 1.71 (2H, quintet, J = 6.6 Hz, H^{2}).

δ_C (100 MHz, CDCl$_3$): 167.6 (C^{18}), 166.8 (C^{11}), 166.3 (C^{4}), 157.7 (C^{21}), 137.4 (C^{16}), 137.0 (C^{13}), 135.2 (C$^{5/9/19}$), 134.1 (C$^{5/9/19}$), 134.0 (C$^{5/9/19}$), 130.7 (C$^{6/8}$), 130.6 (C$^{6/8}$), 129.7 (C^{23}), 129.0 (C^{7}), 128.3 (C^{15}), 127.3 (C^{14}), 124.9 (C^{10}), 119.8 (C^{24}), 118.6 (C^{22}), 113.7 (C^{20}), 78.0 (C^{26}), 75.9 (C^{27}), 55.9 (C^{25}), 49.1 (C^{1}), 43.9 (C^{17}), 43.8 (C^{12}), 37.6 (C^{3}), 28.5 (C^{2}).

***m/z* (ESI):** 525.2245 ([M + H]$^+$ $C_{29}H_{29}N_6O_4$ requires 525.2261).

Alkyne 7. To a solution of **4** (1.91 g, 12.1 mmol) dissolved in dry THF (30 mL) was added DCC (4.98 g, 24.2 mmol) and *N*-hydroxysuccinimide (2.78 g, 24.2 mmol). The reaction was stirred at room temperature under nitrogen for 16 hours. The resulting suspension was filtered under gravity and the solvent removed *in vacuo* to afford a white solid. The crude material was then redissolved in dry CH_2Cl_2 (30 mL) and 4-(Boc-amino) benzylamine (1.38 g, 5.85 mmol) and dry Et_3N (0.96 mL, 7.00 mmol) were added. The solution was stirred at room temperature under nitrogen for 16 hours. The mixture was then washed with aq. 1 M HCl (2 × 20 mL), aq. $NaHCO_3$ (2 × 20 mL) and water (1 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo* to afford a colourless solid. Purification by flash column chromatography (EtOAc : Hexane 1 : 1–2 : 1) gave the *title product* (1.67, 75%) as a clear oil.



***R*$_f$** 0.15 (EtOAc : hexane 1 : 1).

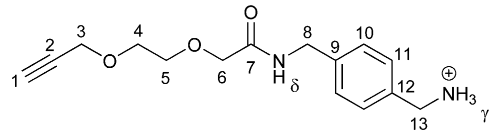
ν_{max}/cm^{-1} (neat): 3330 (C≡C–H), 2976 (C–H), 1664 (C═O), 1515 (C–N), 1095 (C–O–C).

δ_H (400 MHz, CDCl$_3$): 7.30–7.23 (5H, m, H^{10}, H^{11} & NH$^{\delta}$), 4.88 (1H, bs, NH$^{\gamma}$), 4.47 (2H, d, J = 5.9 Hz, H^{8}), 4.31 (2H, d, J = 5.7 Hz, H^{13}), 4.06–4.03 (4H, m, H^{6} & H^{3}), 3.72–3.65 (4H, H^{4} & H^{5}), 2.41 (1H, t, J = 2.4 Hz, H^{1}), 1.46 (9H, s, H^{16}).

δ_C (100 MHz, CDCl$_3$): 169.6 (C^{7}), 155.8 (C^{14}), 138.2 (C^{9}), 137.1 (C^{12}), 128.2 (C^{10}), 127.7 (C^{11}), 79.5 (C^{2}), 79.1 (C^{15}), 74.9 (C^{1}), 70.8 (C^{5}), 70.4 (C^{4}), 68.6 (C^{6}), 58.2 (C^{3}), 44.3 (C^{13}), 42.6 (C^{8}), 28.3 (C^{16}).

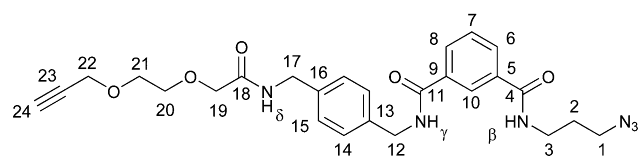
***m/z* (ESI):** 399.1890 ([M + Na]$^+$ $C_{20}H_{28}N_2NaO_5$ requires 399.1890).

Deprotected amine–alkyne salt 10. To a solution of Boc-alkyne **7** (386 mg, 1.03 mmol) in CH_2Cl_2 (5 mL) cooled to 0 °C was added trifluoroacetic acid (1 mL, 3.7 mmol). The solution was warmed to room temperature and stirred for 2 hours, then the volatiles removed *in vacuo*. The product was isolated as the TFA salt. Boc deprotection was confirmed by ^{1}H NMR analysis and the crude material was taken forward immediately without further purification.



δ_H (400 MHz, D$_6$-DMSO): 8.35 (1H, t, J = 6.0 Hz, NH$^{\delta}$), 8.28–7.96 (3H, m, NH$_3^+$), 7.42–7.37 (2H, m, H^{11}), 7.34–7.29 (2H, m, H^{10}), 4.32 (2H, d, J = 6.2 Hz, H^{8}), 4.15 (2H, d, J = 2.3 Hz, H^{3}), 4.01 (2H, q, J = 5.8 Hz, H^{13}), 3.95 (2H, s, H^{6}), 3.65–3.59 (4H, m, H^{4} & H^{5}), 3.44 (1H, t, J = 2.4 Hz, H^{1}).

Alkyne–azide 13. To a solution of **1** (250 mg, 1.00 mmol) dissolved in dry CH_3CN (10 mL) was added DCC (247 mg, 1.20 mmol) and *N*-hydroxysuccinimide (138 mg, 1.20 mmol). The reaction was stirred at room temperature under nitrogen for 16 hours. The resulting suspension was filtered under gravity and the solvent removed *in vacuo* to afford a colourless solid. The crude material was then redissolved in dry CH_2Cl_2 (20 mL) and **10** (390 mg, 1.00 mmol) and dry Et_3N (0.60 mL, 4.4 mmol) were added. The solution was stirred at room temperature under nitrogen for 16 hours. The solution was then washed with aq. 1 M HCl (2 × 20 mL), aq. $NaHCO_3$ (2 × 20 mL) and water (1 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo* to afford a colourless solid. Purification by flash column chromatography (EtOAc : Hexane 6 : 1–8 : 1) gave the *title product* (259 mg, 51%) as a colourless solid.



***R*$_f$** 0.13 (EtOAc : Hexane 4 : 1).

m.p. 78–80 °C.

ν_{max}/cm^{-1} (neat): 3291 (C≡C–H), 3060 (N–H), 2916 (C–H), 2102 (N═N═N), 1649 (C═O), 1530 (C–N), 1097 (C–O–C).

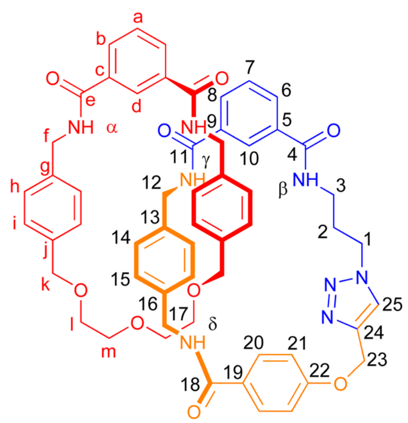
δ_H (400 MHz, CDCl$_3$): 8.22 (1H, s, H^{10}), 8.00–7.92 (2H, m, H^{6} & H^{8}), 7.53 (1H, app. t, H^{7}), 7.34 (1H, bs, NH$^{\delta}$), 7.31–7.22 (4H, m, H^{14} & H^{15}), 6.75–6.66 (2H, m, NH$^{\beta,\gamma}$), 4.61 (2H, d, J = 5.6 Hz, H^{12}), 4.44 (2H, d, J = 5.9 Hz, H^{17}), 4.08 (2H, d, J = 2.4 Hz, H^{22}), 4.03 (2H, s, H^{19}), 3.73–3.66 (4H, m, H^{21} & H^{20}), 3.52 (2H, q, J = 6.6 Hz, H^{3}), 3.42 (2H, t, J = 6.5 Hz, H^{1}), 2.42 (1H, t, J = 2.4 Hz, H^{24}), 1.88 (2H, quintet, J = 6.6 Hz, H^{2}).

δ_C (100 MHz, CDCl$_3$): 169.9 (C^{18}), 166.6 (C^{4}), 166.3 (C^{11}), 137.6 (C^{16}), 137.0 (C^{13}), 134.6 (C$^{5/9}$), 134.5 (C$^{5/9}$), 130.1 (C$^{6/8}$), 130.1 (C$^{6/8}$), 129.0 (C^{7}), 128.2 (C^{14}), 128.1 (C^{15}), 125.2 (C^{10}), 79.1 (C^{23}), 75.0 (C^{24}), 70.5 (C^{19}), 70.0 (C^{20}), 68.7 (C^{21}), 58.3 (C^{22}), 49.4 (C^{1}), 43.9 (C^{12}), 42.5 (C^{17}), 37.8 (C^{3}), 28.7 (C^{2}).

***m/z* (ESI):** 529.2170 ([M + Na]$^+$ $C_{26}H_{30}N_6O_5$ requires 529.2175).

Catenane 15. Macrocycle **14** (60 mg, 0.13 mmol) and alkyne–azide **11** (68 mg, 0.13 mmol) were dissolved in dry CH_2Cl_2

(20 mL) under an argon atmosphere. To the solution, [Cu$(CH_3CN)_4BF_4$] (9.4 mg, 0.03 mmol), TBTA (16 mg, 0.03 mmol) and dry DIPEA (0.022 mL, 0.13 mmol) were added. The reaction was stirred at room temperature for 16 hours. The reaction mixture was diluted with further CH_2Cl_2 (10 mL) and then the solution was washed with 0.02 M EDTA in aq. 1 M NH_3 (2 × 15 mL) and brine (1 × 15 mL). The organic layer was dried ($MgSO_4$) and solvent removed *in vacuo* to afford a yellow solid. Purification by flash column chromatography (CH_2Cl_2:CH_3OH 98 : 2) gave the *title product* (76 mg, 59%) as a colourless solid.



R R_f 0.29 (CH_2Cl_2:CH_3OH 98 : 2).

m.p. 165–167 °C.

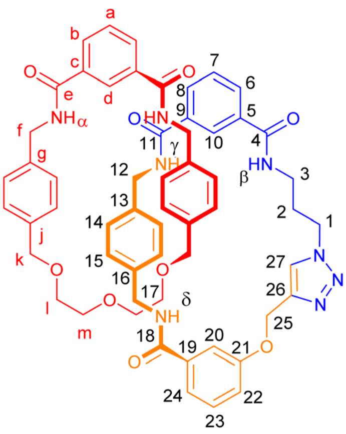
ν_{max}/cm^{-1} (neat): 3345 (N–H), 2868 (C–H), 1630 (C═O), 1578 (C–N), 1533 (C–N), 1416 (Ar-C).

δ_H (400 MHz, 50 : 50 $CDCl_3$/CD_3OD): 8.70 (1H, s, H^d), 8.21–8.16 (2H, m, H^b), 8.11 (1H, d, J = 7.7 Hz, $H^{6/8}$), 8.02 (1H, d, J = 7.8 Hz, $H^{6/8}$), 7.82–7.72 (3H, m, H^{20} & H^{25}), 7.68–7.59 (2H, m, H^7 & H^a), 7.52 (1H, s, H^{10}), 7.40 (2H, d, J = 7.9 Hz, H^{14}), 7.07–6.97 (4H, m, H^{15} &H^{21}), 6.94 (4H, d, J = 7.9 Hz, H^h), 6.56 (4H, d, J = 7.9 Hz, H^i), 5.42 (2H, s, H^{23}), 4.58 (2H, dd, J = 14.2, 5.1 Hz, H^f), 4.47–4.36 (4H, m, H^{12} & $H^{f'}$), 4.25 (2H, bs, H^1), 3.97–3.79 (6H, m, H^k, $H^{k'}$ & H^{17}), 2.98 (2H, bs, H^3), 2.93–2.75 (4H, m, H^l), 2.64–2.48 (4H, m, H^m), 1.84 (2H, bs, H^2).

δ_C (100 MHz, 50 : 50 $CDCl_3$/CD_3OD): 167.4 (C^e), 167.0 (C^4), 166.4 (C^{18}), 166.3 (C^{11}), 159.8 (C^{22}), 143.4 (C^{24}), 139.3 (C^{13}), 139.2 (C^{16}), 135.2 (C^j), 133.9 (C^c), 133.9 ($C^{5/9}$), 133.8 ($C^{5/9}$), 133.5 ($C^{6/8}$), 131.8 ($C^{6/8}$), 131.6 (C^b), 131.5 (C^g), 129.6 (C^i), 129.3 (C^{15}), 129.3 (C^{14}), 128.9 (C^a), 128.9 (C^7), 128.7 (C^{20}), 128.1 (C^h), 126.3 (C^{19}), 124.6 (C^d) 124.6 (C^{10}), 123.4 (C^{25}) 115.3 (C^{21}), 73.4 (C^k), 69.9 (C^m), 68.4 (C^l), 60.5 (C^{23}), 47.9 (C^1), 44.3 (C^f), 43.4 (C^{17}), 43.2 (C^{12}), 37.4 (C^3), 29.5 (C^2).

***m*/*z* (ESI):** 999.4400 ([M + H]$^+$ $C_{57}H_{59}N_8O_9$ requires 999.4426).

Catenane 16. Macrocycle **14** (60 mg, 0.13 mmol) and alkyne–azide **12** (68 mg, 0.13 mmol) were dissolved in dry CH_2Cl_2 (20 mL) and placed under an argon atmosphere. To the solution, [Cu$(CH_3CN)_4BF_4$] (9.4 mg, 0.03 mmol), TBTA (16 mg, 0.03 mmol) and dry DIPEA (0.022 mL, 0.13 mmol) were added. The reaction was stirred at room temperature for 16 hours. The reaction mixture was diluted with further CH_2Cl_2 (10 mL) and then the solution was washed with 0.02 M EDTA in aq. 1 M NH_3 (2 × 15 mL) and brine (1 × 15 mL). The combined organic layers were dried ($MgSO_4$) and solvent removed *in vacuo* to afford a yellow solid. Purification by flash column chromatography (CH_2Cl_2:CH_3OH 98 : 2) gave the *title product* (79 mg, 60%) as a colourless solid.



R_f 0.29 (CH_2Cl_2:CH_3OH 98 : 2).

m.p. 168–170 °C.

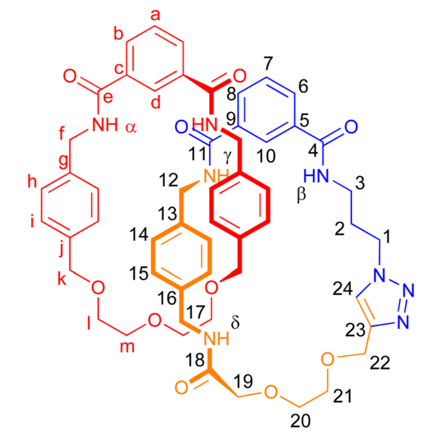
ν_{max}/cm^{-1} (neat): 3341(N–H), 2868 (C–H), 1630 (C═O), 1578 (C–N), 1533 (C–N), 1416 (Ar–C).

δ_H (400 MHz, 50 : 50 $CDCl_3$/CD_3OD): 8.71 (1H, s, H^d), 8.19 (2H, dd, J = 7.8 Hz, H^b), 8.12 (1H, d, J = 7.7 Hz, $H^{6/8}$), 8.05 (1H, d, J = 7.8 Hz, $H^{6/8}$), 7.80 (1H, s, H^{27}), 7.69–7.63 (2H, m, H^7 & H^a), 7.62 (1H, s, H^{10}), 7.51 (1H, d, J = 7.5 Hz, H^{24}), 7.43–7.35 (3H, m, H^{23} & H^{14}), 7.32 (1H, s, H^{20}), 7.22 (1H, dd, J = 7.2, 2.4 Hz, H^{22}), 7.04 (2H, d, J = 7.7 Hz, H^{15}), 6.94 (4H, d, J = 7.9 Hz, H^h), 6.56 (4H, d, J = 7.9 Hz, H^i), 5.34 (2H, s, H^{25}), 4.59 (2H, d, J = 14.2 Hz, H^f), 4.47–4.35 (4H, m, H^{12} & $H^{f'}$), 4.26 (2H, bs, H^1), 3.98–3.90 (4H, m, H^k & $H^{k'}$), 3.88 (2H, bs, H^{17}), 3.07–2.92 (8H, m, H^l, $H^{l'}$, H^m & H^3), 2.78–2.71 (2H, m, $H^{m'}$), 1.96 (2H, bs, H^2).

δ_C (100 MHz, 50 : 50 $CDCl_3$/CD_3OD): 167.8 (C^e), 166.5 (C^{18}), 166.4 (C^{11}), 165.8 (C^4), 157.24 (C^{21}), 143.4 (C^{26}), 144.3 ($C^{5/9}$), 138.4 ($C^{5/9}$), 137.1 (C^j), 136.7 ($C^{16/19/c}$), 136.5 (C^{13}), 135.0 (C^g), 134.6 ($C^{16/19/c}$), 131.6 ($C^{6/8}$), 131.6 ($C^{6/8}$), 131.6 (C^b), 130.0 (C^{23}), 129.8 (C^i) 129.5 (C^{15}) 129.3 (C^{14}) 129.1 (C^a), 129.0 (C^7), 128.4 (C^h), 124.6 (C^{10}), 124.6 (C^d), 123.1 (C^{27}), 119.3 (C^{24}), 117.3 (C^{22}), 114.7 (C^{20}), 72.9 (C^k), 69.9 (C^l), 68.5 (C^m), 60.9 (C^{25}), 52.8 (C^1), 43.6 (C^f), 42.8 (C^{12}), 42.7 (C^{17}), 36.3 (C^1), 29.2 (C^2).

***m*/*z* (ESI):** 999.4400 ([M + H]$^+$ $C_{57}H_{59}N_8O_9$ requires 999.4427).

Catenane 17. Macrocycle **14** (60 mg, 0.13 mmol) and alkyne–azide **13** (63 mg, 0.13 mmol) were dissolved in dry CH_2Cl_2 (20 mL) and placed under an argon atmosphere. To the solution, [Cu$(CH_3CN)_4BF_4$] (9.4 mg, 0.03 mmol), TBTA (16 mg, 0.03 mmol) and dry DIPEA (0.022 mL, 0.13 mmol) were added. The reaction was stirred at room temperature for 16 hours. The reaction mixture was diluted with further CH_2Cl_2 (10 mL) and then the solution was washed with 0.02 M EDTA in aq. 1 M NH_3 (2 × 15 mL) and brine (1 × 15 mL). The combined organic layers were dried ($MgSO_4$) and solvent removed *in* *vacuo* to afford a yellow solid. Purification by flash column chromatography (CH_2Cl_2 : CH_3OH 96 : 4–94 : 6) gave the *title product* (89 mg, 70%) as a colourless solid.



R_f 0.32 (CH_2Cl_2 : CH_3OH 96 : 4).

m.p. 118–121 °C.

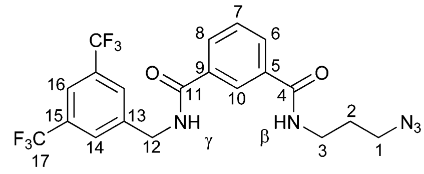
ν_{max}/cm^{-1} **(neat):** 3215 (C–H), 2860 (C–H), 1638 (C=O), 1522 (C–N), 1017 (C–O–C).

δ_H **(400 MHz, 50 : 50 $CDCl_3$/CD_3OD):** 8.70 (1H, s, H^d), 8.18 (2H, dd, J = 7.8, 1.8 Hz, H^b), 8.13 (1H, d, J = 7.7 Hz, $H^{6/8}$), 8.05 (1H, d, J = 7.8 Hz, $H^{6/8}$), 7.80 (1H, s, H^{24}), 7.70–7.63 (3H, m, H^7 & H^a), 7.62 (1H, s, H^{10}), 7.26 (2H, d, J = 8.1 Hz, H^{14}), 7.03 (2H, d, J = 8.1 Hz, H^{15}), 6.96 (4H, d, J = 7.9 Hz, H^h), 6.63 (4H, d, J = 7.9 Hz, H^i), 4.63–4.53 (4H, m, H^{22} & H^f), 4.42–4.36 (4H, m, $H^{f'}$ & H^{12}), 4.32 (2H, bs, H^1), 4.11–4.02 (4H, m, H^k), 3.98 (2H, m, H^{19}), 3.90 (2H, bs, H^{17}), 3.71 (4H, bs, H^{20} & H^{21}), 3.15–3.00 (8H, dt, m, H^l, H^3, H^m & $H^{l'}$), 2.90–2.85 (2H, m, $H^{m'}$), 2.08 (2H, bs, H^2).

δ_C **(100 MHz, 50 : 50 $CDCl_3$/CD_3OD):** 170.0 (C^{18}), 167.4 (C^e), 167.0 (C^4), 166.4 (C^{11}), 144.3 (C^{23}), 138.7 (C^{16}),138.4 ($C^{5/9/c}$), 138.3 ($C^{5/9/c}$), 137.1 ($C^{5/9/c}$), 136.9 (C^{13}), 135.4 (C^j), 131.7 (C^b) 131.6 ($C^{6/8}$), 131.4 ($C^{6/8}$), 131.2 (C^g), 129.5 (C^i) 129.3 (C^{15}), 129.1 (C^a), 128.7 (C^7), 128.5 (C^{14}), 128.2 (C^h), 124.8 (C^{10}), 124.6 (C^d), 123.6 (C^{24}), 73.5 (C^k), 70.4 (C^{19}), 70.3 (C^m), 70.2 (C^{21}), 69.7 (C^{20}) 68.7 (C^l), 64.2 (C^{22}), 47.5 (C^1), 44.2 (C^f), 43.3 (C^{17}), 42.1 (C^{12}), 36.6 (C^3), 29.5 (C^2).

***m/z* (ESI):** 1003.4325 ($[M + H]^+$ $C_{54}H_{61}N_8O_{10}$ requires 1003.4372).

Azide 18. To a solution of **1** (100 mg, 0.40 mmol) in dry CH_3CN (15 mL) under an argon atmosphere was added DCC (99 mg, 0.48 mmol) and *N*-hydroxysuccinimide (55 mg, 0.48 mmol). The reaction mixture was stirred at room temperature for 16 hours. The resulting suspension was filtered under gravity and the solvent removed *in vacuo*. The resulting crude material was re-dissolved in dry CH_2Cl_2 (20 mL). 3,5-Bis(trifluoromethyl)benzylamine (117 mg, 0.48 mmol) and Et_3N (0.11 mL, 0.80 mmol) were then added, and the reaction mixture was stirred at room temperature overnight under an argon atmosphere. The reaction mixture was then washed with aq. 1 M HCl (2 × 15 mL) and aq. $NaHCO_3$ (2 × 15 mL). The organic layer was dried ($MgSO_4$) and solvent removed *in vacuo*. The crude material was purified by silica gel column chromatography (EtOAc/hexane 1 : 1) to afford the *title product* as a waxy clear oil (129 mg, 68%).



R_f 0.15 (EtOAc : Hexane 3 : 7).

ν_{max}/cm^{-1} **(neat):** 3330 (CH_2), 2933 (ArCH), 2096 (N=N=N), 1638 (C=O), 1531 (C–N).

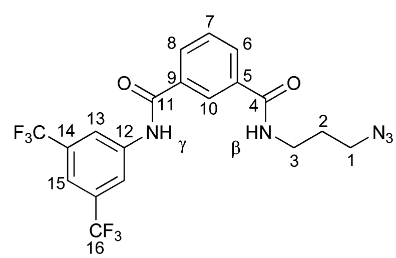
δ_H **(400 MHz, $CDCl_3$):** 8.23 (1H, s, H^{10}), 8.01–7.96 (1H, m, H^8), 7.93–7.88 (1H, m, H^6), 7.80 (3H, s, H^{14} & H^{16}), 7.54 (1H, app. t, H^7), 6.95 (1H, bs, NH^γ), 6.54 (1H, bs, NH^β), 4.77 (2H, d, J = 6.1 Hz, H^{12}), 3.56 (2H, t, J = 6.6 Hz, H^3), 3.45 (2H, t, J = 6.5 Hz, H^1), 1.91 (2H, quintet, J = 6.6 Hz, H^2).

δ_C **(100 MHz, $CDCl_3$):** 166.6 (C^{11}), 166.5 (C^4), 140.7 (C^{13}), 134.8 (C^9), 134.0 (C^5), 131.9 (q, ^2J = 34 Hz, C^{15}), 130.2 (C^8), 130.0 (C^6), 129.2 (C^7), 128.0 (C^{14}), 125.5 (C^{10}), 124.6 (C^{16}), 121.9 (q, ^1J = 271 Hz, C^{17}), 49.5 (C^1), 43.4 (C^{12}), 38.0 (C^3), 28.7 (C^2).

δ_F (377 MHz, $CDCl_3$): −62.8

***m/z* (ESI):** 474.1359 ($[M + H]^+$ $C_{20}H_{18}N_5O_2F_6$ requires 474.1346).

Azide 19. To a solution of **1** (95 mg, 0.38 mmol) in dry CH_3CN (15 mL) under an argon atmosphere was added DCC (95 mg, 0.46 mmol) and *N*-hydroxysuccinimide (52 mg, 0.46 mmol). The reaction mixture was stirred at room temperature for 16 hours maintaining the argon atmosphere. The resulting suspension was filtered under gravity and excess CH_3CN removed *in vacuo*. The resulting crude material was re-dissolved in CH_2Cl_2 (20 mL). 3.5-Bis(trifluoromethyl)aniline (110 mg, 0.42 mmol) and Et_3N (0.11 mL, 0.80 mmol) were then added, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was then washed with 1 M HCl (2 × 15 mL) and $NaHCO_3$ (2 × 15 mL). The organic layer was dried ($MgSO_4$) and solvent removed *in vacuo*. The crude material was purified by silica gel column chromatography (EtOAc/hexane 1 : 1) to afford the *title product* as a brown oil (89 mg, 51%).



R_f 0.17 (EtOAc : hexane 3 : 7).

ν_{max}/cm^{-1} **(neat):** 3330 (N–H), 2935 (ArCH), 2096 (N=N=N), 1638 (C=O), 1531 (C–N).

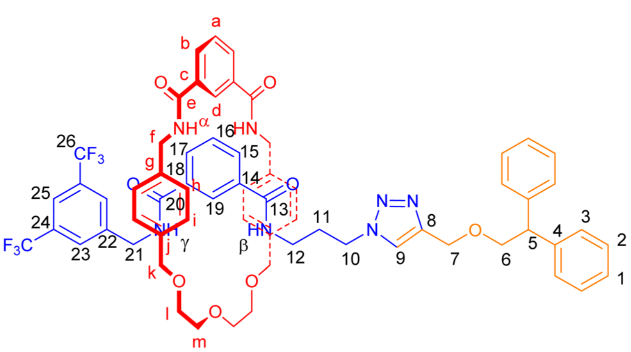
***δ*~H~ (400 MHz, D~6~-DMSO):** 10.99 (1H, bs, NH$^{\gamma}$), 8.72 (1H, bs, NH$^{\beta}$), 8.55 (2H, s, H^{13}), 8.49 (1H, s, H^{15}), 8.15 (1H, d, J = 7.1 Hz, H^{6}), 8.10 (1H, d, J = 7.2 Hz, H^{8}), 7.84 (1H, s, H^{10}), 7.68 (1H, t, J = 7.8 Hz, H^{7}), 3.45 (2H, t, J = 6.5 Hz, H^{3}), 3.38 (2H, t, J = 6.5 Hz, H^{1}), 1.82 (2H, quintet, J = 6.6 Hz, H^{2}).

δ_C (100 MHz, D$_6$-DMSO): 166.3 (C^{11}), 166.1 (C^{4}), 141.4 (C^{12}), 135.4 (C^{9}), 134.5 (C^{5}), 131.3 (q, ^2J = 34 Hz, C^{14}), 131.1 (C^{7}), 130.9 (C^{15}), 129.1 (C^{6}), 127.2 (C^{8}), 122.3 (C^{13}), 120.3 (q, ^1J = 271 Hz, C^{16}), 117.3 (C^{10}), 48.9 (C^{1}), 37.2 (C^{3}), 28.8 (C^{2}).

δ_F (377 MHz, D$_6$-DMSO): −61.6.

***m*/*z* (ESI):** 458.1057 ([M − H]$^-$ $C_{19}H_{16}F_6N_5O_2$ requires 458.1065).

Rotaxane 21. Macrocycle **14** (20 mg, 0.042 mmol) and azide **18** (21 mg, 0.046 mmol) were dissolved in dry CH_2Cl_2 (1 mL) under an argon atmosphere. Then alkyne **20** (12 mg, 0.046 mmol), [Cu(CH$_3$CN)$_4$BF$_4$] (1.4 mg, 0.004 mmol), TBTA (2.4 mg, 0.004 mmol) and dry DIPEA (9 μL, 6.6 mg, 0.051 mmol) were added. The reaction was stirred at RT for 18 hours maintaining the argon atmosphere. Then, the reaction was diluted to 10 mL, washed with 0.02 M EDTA in aq. 1 M NH_3 (2 × 10 mL) and brine (1 × 10 mL). The organic layer was dried ($MgSO_4$), filtered and solvent removed *in vacuo*. The crude material was purified by preparative TLC (repeated running in 96 : 2 : 3 CH_2Cl_2/CH_3OH/CH_3COCH_3) which allowed for isolation of the product with contaminated macrocycle **14**. Pure rotaxane was isolated after running another preparative TLC (run twice in 95 : 2 : 3 CH_2Cl_2/CH_3OH/CH_3COCH_3) to give the *title product* as a colourless glassy film (14 mg, 29%).



R_f 0.59 (CH_2Cl_2 : CH_3OH 96 : 4).

ν_{max}/cm^{-1} (neat): 3332 (N–H), 2929 (C–H), 2862 (C–H),1638 (C=O), 1528 (C–N), 1276 (C–O).

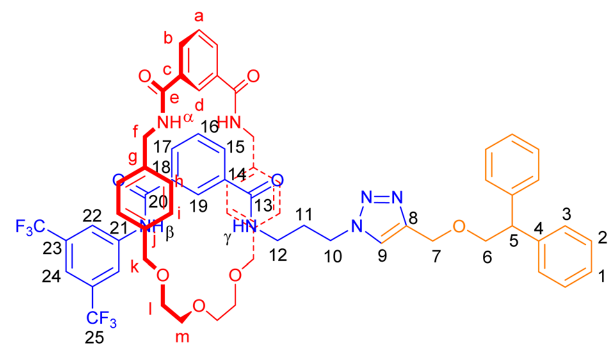
δ_H (400 MHz, CDCl$_3$): 8.66 (1H, s, H^{d}), 8.31–8.21 (3H, m, H^{b} & H$^{15/17}$), 8.07 (1H, bs, H$^{15/17}$), 7.84 (1H,s, H^{25}), 7.78 (2H, bs, H^{23}), 7.73 (2H, m, H^{16} & H^{19}), 7.62 (1H, t, J = 7.8 Hz, H^{a}), 7.56 (2H, bs, NH$^{\alpha}$), 7.32–7.16 (11H, m, H^{1}, H^{2}, H^{3} & H^{9}), 6.84 (4H, d, J = 7.9 Hz, H^{h}), 6.53 (4H, d, J = 8.0 Hz, H^{i}), 4.64 (2H,s, H^{7}), 4.59–4.37 (4H, m, H^{f}), 4.32 (1H, t, J = 7.7 Hz, H^{5}), 4.14–4.02 (8H, m, H^{6}, H^{k} &H^{10}), 3.97 (2H, bs, H^{21}), 3.70–3.55 (2H, m, H^{l}), 3.44–3.30 (4H, m, H^{m} & H$^{l'}$), 3.28–3.20 (2H, m, H$^{m'}$), 2.78 (2H, bs, H^{12}), 1.78 (2H, bs, H^{11}).

δ_C (100 MHz, CDCl$_3$): 166.9 (C^{13}), 166.6 (C^{20}), 166.4 (C^{e}), 145.2 (C^{8}), 141.9 (C^{4}), 136.4 (C^{g}), 134.8 (C^{j}), 133.8 (C$^{14/18/22}$), 133.7 (C$^{14/18/22}$), 133.1 (C$^{14/18/22}$), 132.1 (C^{24}), 132.0 (C^{b}), 131.8 (C$^{15/17}$), 131.6 (C$^{15/17}$), 129.9 (C^{i}), 129.5 (C^{a}), 129.2 (C^{23}), 128.8 (C^{16}), 128.4 (C^{3}), 128.3 (C^{h}), 128.2 (C^{2}), 126.5 (C^{1}), 124.5 (C^{25}), 123.8 (C^{d}), 122.6 (C^{9}), 121.7 (C^{19}), 73.9 (C^{k}), 73.7 (C^{6}), 70.7 (C^{m}), 68.8 (C^{l}), 64.5 (C^{7}), 50.9 (C^{5}), 47.6 (C^{10}), 44.5 (C^{f}), 43.3 (C^{21}), 36.8 (C^{12}), 29.6 (C^{11}).

δ_F (377 MHz, CDCl$_3$): −62.6.

***m*/*z* (ESI):** 1184.4715 ([M + H]$^+$ $C_{65}H_{64}F_6N_7O_8$ requires 1184.4752).

Rotaxane 23. Macrocycle **14** (20 mg, 0.042 mmol) and azide **19** (21 mg, 0.046 mmol) were dissolved in dry CH_2Cl_2 (1 mL) under an argon atmosphere. Then alkyne **20** (12 mg, 0.046 mmol), [Cu(CH$_3$CN)$_4$BF$_4$] (1.4 mg, 0.004 mmol), TBTA (2.4 mg, 0.004 mmol) and dry DIPEA (9 μL, 6.6 mg, 0.051 mmol) were added. The reaction was stirred at RT for 18 hours maintaining the argon atmosphere. Then, the reaction was diluted to 10 mL, washed with 0.02 M EDTA in aq. 1 M NH_3 solution (2 × 10 mL) and brine (1 × 10 mL). The organic layer was dried ($MgSO_4$), filtered and solvent removed *in vacuo*. The crude material was purified by preparative TLC (repeated running in 98 : 2 CH_2Cl_2/CH_3OH) which allowed for isolation of the product with contaminated macrocycle **14**. Pure rotaxane was isolated after running another preparative TLC (repeated running in 96 : 2 : 2 CH_2Cl_2/CH_3OH/CH_3COCH_3) to give the *title product* as a colourless glassy film (20 mg, 40%).



R_f 0.64 (CH_2Cl_2:CH_3OH 96 : 4).

ν_{max}/cm^{-1} (neat): 3319 (N–H), 2918 (C–H), 1645 (C=O), 1528 (C–N), 1276 (C–O).

δ_H (400 MHz, CDCl$_3$): 8.55 (1H, s, H^{d}), 8.32–8.22 (3H, m, H^{b} & H$^{15/17}$), 8.06–7.87 (3H, m, H$^{15/17}$ & H^{19}), 7.84 (1H, bs, H^{22}), 7.72–7.62 (2H, m, H^{16} & H^{a}), 7.58 (1H, s, H^{24}), 7.43–7.17 (13H, m, H^{1}, H^{2}, H^{3}, H^{9} & NH$^{\alpha}$), 6.78 (4H, d, J = 7.9 Hz, H^{h}), 6.54 (4H, d, J = 8.0 Hz, H^{i}), 4.67 (2H, s, H^{7}), 4.52–4.36 (4H, m, H^{f}), 4.34–4.20 (3H, m, H^{5} & H^{10}), 4.18–4.10 (4H, m, H^{k}), 4.09 (2H, d, 7.3 Hz, H^{6}), 3.79–3.72 (2H, m, H^{m}), 3.68–3.60 (2H, m, H$^{m'}$), 3.55–3.44 (4H, m, H^{l}), 3.33 (2H, bs, H^{12}), 2.14 (2H, bs, H^{11}).

δ_C (100 MHz, CDCl$_3$): 166.3 (C^{e}), 166.2 (C^{20}), 165.7 (C^{13}), 145.3 (C^{8}), 141.9 (C$^{18/14}$), 139.4 (C$^{21/c}$), 137.4 (C^{j}), 134.8 (C^{g}), 133.7 (C$^{14/18}$), 133.7 (C$^{21/c}$), 132.8 (C$^{15/17}$), 132.0 (C$^{15/17}$), 131.9 (C^{b}), 129.4 (C^{a}), 129.4 (C^{4}), 129.3 (C^{i}), 129.0 (C^{16}), 128.5 (C^{22}), 128.4 (C^{2}), 128.2 (C^{3}), 128.2 (C^{h}), 126.5 (C^{1}), 124.8 (C^{22}), 123.1 (C^{d}), 122.7 (C^{9}), 121.6 (C^{19}), 117.0 (C^{24}), 73.9 (C^{k}), 73.7 (C^{6}), 70.6 (C^m), 68.8 (C^l), 64.6 (C^7), 50.9 (C^5), 47.8 (C^{10}), 44.4 (C^f), 37.1 (C^{12}), 29.7 (C^{11}).

δ_F (377 MHz, $CDCl_3$): −63.0.

***m*/*z* (ESI):** 1170.4559 ($[M + H]^+$ $C_{64}H_{62}F_6N_7O_8$ requires 1170.4595).

Author contributions

NHE proposed the study. NHE conducted initial experiments (see ESI†). SRB conducted the synthesis, characterization and analysis of all materials in the main article with assistance from GRA. NHE supervised the work. SRB and NHE wrote the manuscript. All authors discussed and commented on the manuscript.

Conflicts of interest

There are no conflicts to declare.

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Underlying data for this paper are provided in the Experimental section and ESI.† Electronic copies of NMR spectra (including fid files) will be available upon publication from: https://doi.org/10.17635/lancaster/researchdata/554, https://doi.org/10.17635/lancaster/researchdata/569, https://doi.org/10.17635/lancaster/researchdata/570, https://doi.org/10.17635/lancaster/researchdata/574.

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17 The corresponding author had previously prepared (but not reported) [2]catenane **15**, preparing precursor **11** by a different route. See ESI pp. S48–S67 for details.†
18 To date it has not been possible to isolate pure samples of the macrocyclic product arising from cyclization of **11–13**.
19 By analogous reactions (in the absence of macrocycle **14**), non-interlocked axles **22** and **24** were also prepared (in 80% and 79% yield respectively) to aid ^{1}H NMR spectroscopic interpretation (see ESI pp. S3–S5†).
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