Chemical Consequences of the Mechanical Bond: A Tandem Active Template-Rearrangement Reaction

Florian Modicom*, Ellen M. G. Jamieson*, Elise Rochette, and Stephen M. Goldup*

anie_201813950_sm_misellaneous_information.pdf
1. General Experimental

2. Synthesis of substrates
   3,5-Di-tert-butylbenzaldehyde (S1)
   1-(3,5-Di-tert-butylphenyl)prop-2-yn-1-ol (3a)
   1,3-Di-tert-butyl-5-(1-methoxyprop-2-yn-1-yl)benzene (3d)
   1-(3,5-Di-tert-butylphenyl)ethan-1-one (S2)
   2-(3,5-Di-tert-butylphenyl)but-3-yn-2-ol (3c)
   1,3-Di-tert-butyl-5-(prop-2-yn-1-yl)benzene (3e)
   1-(3,5-Di-tert-butylphenyl)but-3-yn-2-ol (3b)

3. Synthesis of acrylamide rotaxanes
   General Procedure A
   Rotaxane 5
   Rotaxane 6
   Rotaxane 7
   Rotaxane 8
   Rotaxane 9
   Rotaxane 10
   Rotaxane 11

4. Synthesis of triazole rotaxanes
   General Procedure B
   Rotaxane 4
   Rotaxane 54
   Rotaxane 55
   Rotaxane 56
   Rotaxane 57
   Rotaxane 58
   Rotaxane 59
   Rotaxane 60
   Rotaxane 61
   Axle 52
   Thread 53

5. Single crystal X-ray analysis of rotaxanes 4, 5, 6 and 8

6. Optimisation of reaction conditions for the rearrangement reaction

7. Kinetic Study of the reaction of 1a, 2a and 3a.

8. Control experiments: axle formation under conditions optimised for the formation of acrylamide rotaxane 5

9. Mechanistic studies: rearrangement of triazolide 12 under aqueous conditions

10. Mechanistic studies: rearrangements triggered by Tf₂O under anhydrous conditions
    i. In situ ¹H NMR analysis of the reaction of the product of 1a, 2a and 3c with Tf₂O
    ii. In situ ¹H NMR analysis of the reaction of 1a, 2a and 3a followed by Tf₂O

11. Preliminary computational analysis of the mechanism of the rearrangement process
    i. Preparation of a truncated model 1a of triazolide S15
    ii. DFT evaluation of the pathway of N₂ loss from truncated triazolide model 1a
    iii. DFT evaluation of the pathway of N₂ loss from truncated triazole model 1b
    iv. Conclusions

12. References
1. General Experimental

**Synthesis:** Unless otherwise stated, all reagents, including anhydrous solvents, were purchased from commercial sources and used without further purification. All reactions were carried out under an atmosphere of N$_2$ using anhydrous solvents unless otherwise stated. Petrol refers to the fraction of petroleum ether boiling in the range 40–60 °C. EDTA-NH$_3$ solution refers to an aqueous solution of NH$_3$ (17% w/w) with 0.1 M sodium-ethylenediaminetetraacetate. Flash column chromatography was performed using Biotage Isolera-4 or Biotage Isolera-1 automated chromatography system, employing Biotage SNAP or ZIP cartridges. Analytical TLC was performed on precoated silica gel plates (0.25 mm thick, 60F254, Merck, Darmstadt, Germany) and observed under UV light or with potassium permanganate solution. Microwave heating of reactions was achieved using a Biotage Initiator+ microwave system. Reactions were run at a maximum power level of 400 W in crimp-cap sealed vials (CEM Ltd.). The temperature was monitored automatically and maintained at the set level throughout the reaction after an initial ramp period, typically ~ 1 minute.

**Analysis:** NMR spectra were recorded on Bruker AV400, AV3-400 or AV500 instrument, at a constant temperature of 298 K. Chemical shifts are reported in parts per million from low to high field and referenced to residual solvent. Coupling constants (J) are reported in Hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: m = multiplet, quint = quintet, q = quartet, t = triplet, d = doublet, s = singlet, app. = apparent, br = broad. Signal assignment was carried out using 2D NMR methods (HSQC, HMBC, COSY, NOESY) where necessary. All melting points were determined using a Griffin apparatus. Low resolution mass spectrometry was carried out by the mass spectrometry services at the University of Southampton (Waters TQD mass spectrometer equipped with a triple quadrupole analyser with UHPLC injection [BEH C18 column; MeCN-hexane gradient {0.2% formic acid}]). High resolution mass spectrometry was carried out by the mass spectrometry services at the University of Southampton (MaXis, Bruker Daltonics, with a Time of Flight (TOF) analyser; samples were introduced to the mass spectrometer via a Dionex Ultimate 3000 autosampler and uHPLC pump in a gradient of 20% acetonitrile in hexane to 100% acetonitrile (0.2% formic acid) over 5 min at 0.6 mL min; column: Acquity UPLC BEH C18 (Waters) 1.7 micron 50 × 2.1 mm).

The following compounds were synthesised according to literature procedures:

- 2-(3,5-di-tert-butylphenyl)acetaldehyde **S3**, [1]
- 1-azido-3,5-di-tert-butylbenzene **2a**, [2]
- 1-(azidomethyl)-3,5-di-tert-butylbenzene **2b**, [3]
- 1-((3-azidopropoxy)methyl)-3,5-di-tert-butylbenzene **2c**, [4]
- Macrocycle **1a**, **1b**, **1c** and **1d**. [5]
2. Synthesis of substrates

3,5-Di-tert-butylbenzaldehyde (S1)

3,5-Di-tert-butyltoluene (6.1 g, 29.9 mmol) was treated with NBS (11.0 g, 62.0 mmol) and AIBN (33.8 mg, 0.2 mmol) in PhCl (150 mL), and stirred for 16 h at 140 °C. The mixture was cooled to rt and passed through a Celite plug. The solvent was removed in vacuo. The residue was slurried in 20 mL of 1:1 water/ethanol. Hexamethylenetetramine (12.2 g, 86.9 mmol) was added, and the mixture was heated to reflux for 4 h, cooled to rt, diluted with PhMe-Et₂O (1:1, 130 mL) and the phases separated. The organic phase was washed with brine (50 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Chromatography (petrol/Et₂O 95:5) gave S1 as a white solid (5.0 g, 77%). M.p. 84 - 86 °C. Spectra were consistent with those previously reported. [6] ¹H NMR (400 MHz, CDCl₃) δ: 10.01 (s, 1H, H₃), 7.75-7.68 (m, 3H, H₈ and H₉), 1.37 (s, 18H, H₄). ¹³C NMR (101 MHz, CDCl₃) δ: 193.3, 152.0, 136.3, 129.9, 124.2, 35.2, 31.3.

Figure S1 ¹H NMR (CDCl₃, 400 MHz) of S1
S1 (1.4 g, 6.4 mmol) was dissolved in THF (20 mL) at 0 °C under N₂. Ethynylmagnesium chloride (0.6 M in THF, 10 mmol, 16 mL) was added dropwise. The mixture was stirred for 20 h at rt. Saturated NH₄Cl(aq) (10 mL) was added and the solvent removed in vacuo. The residue was extracted with Et₂O (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Chromatography (petrol/ethyl acetate 9:1) gave 3a as a light-yellow oil (1.5 g, 97%). ¹H NMR (400 MHz, CDCl₃) δ: 7.44-7.39 (m, 3H, H₆, H₇), 5.46 (d, J = 2.2, 1H, H₁), 2.67 (d, J = 2.2, 1H, H₁), 2.14 (br. s, 1H, H₃), 1.34 (s, 18H, H₄). ¹³C NMR (101 MHz, CDCl₃) δ: 151.2, 139.3, 122.7, 121.0, 84.1, 74.7, 65.1, 35.0, 31.6. HR-EI-MS m/z = 244.18118 M⁺ (calc. for C₁₁H₂₂O 244.18217).

Figure S2]JMOD NMR (CDCl₃ 101 MHz) of S1

1-(3,5-Di-tert-butylphenyl)prop-2-yn-1-ol (3a)
Figure S3: $^1$H NMR (CDCl$_3$, 400 MHz) of 3a

Figure S4: JMOD NMR (CDCl$_3$, 101 MHz) of 3a
1,3-Di-tert-butyl-5-(1-methoxyprop-2-yn-1-yl)benzene (3d)

3a (50 mg, 0.2 mmol) was dissolved in THF (1 mL) at 0 °C under N₂. NaH (12 mg, 0.3 mmol) was added in one portion. The mixture was stirred for 10 minutes and MeI (26 μL, 0.4 mmol) was added. The mixture was stirred for 3 h at rt. Saturated NH₄Cl(aq) (5 mL) was added and the mixture extracted with Et₂O (3 × 10 mL). The combined organic layers were washed with brine (5 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Chromatography (petrol/Et₂O 95:5) gave 3d as a yellow oil (52 mg, 98%). ¹H NMR (400 MHz, CDCl₃) δ: 7.40 (t, J = 1.8, 1H, H₆), 7.34 (d, J = 1.8, 2H, H₅), 5.05 (d, J = 2.2, 1H, H₄), 3.47 (s, 3H, H₃), 2.65 (d, J = 2.2, 1H, H₂), 1.33 (s, 18H, H₁). ¹³C NMR (101 MHz, CDCl₃) δ: 151.1, 137.1, 122.9, 81.9, 75.7, 73.7, 56.3, 35.1, 31.6. HR-EI-MS m/z = 258.19835 M⁺ (calc. for C₁₈H₂₆O 258.19782).

Figure S5 ¹H NMR (CDCl₃, 400 MHz) of 3d
Figure S6 $^{13}$C NMR (CDCl$_3$, 101 MHz) of 3d

1-(3,5-Di-tert-butylphenyl)ethan-1-one (S2)

3,5-Di-tert-butylbenzoic acid (470 mg, 2 mmol) was dissolved in THF (5 mL) at -78 °C under N$_2$. MeLi (1.6 M in Et$_2$O, 2.75 mL, 4.4 mmol) was added dropwise. The mixture was slowly warmed to rt and stirred for 30 minutes then saturated NH$_4$Cl(aq) (10 mL) was added and the mixture extracted with petrol (3 × 20 mL), dried (MgSO$_4$), filtered and the solvent removed \textit{in vacuo}. Chromatography (petrol/ethyl acetate 95:5) gave S2 as a colourless oil (370 mg, 80%). Spectra were consistent with those previously reported.\[1\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.81 (t, $J$ = 1.8, 1H, H$_B$), 7.65 (d, $J$ = 1.8, 2H, H$_C$), 2.61 (s, 3H, H$_D$), 1.36 (s, 18H, H$_A$). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$: 199.1, 151.4, 137.0, 127.5, 122.7, 35.1, 31.5, 29.9.
Figure S7 $^1$H NMR (CDCl$_3$, 400 MHz) of S2

Figure S8 $^{13}$C NMR (CDCl$_3$, 101 MHz) of S2
S2 (370 mg, 1.6 mmol) was dissolved in THF (3 mL) at 0 °C under N₂. Ethynylmagnesium chloride (0.6 M in THF, 2.4 mmol, 4 mL) was added dropwise. The mixture was stirred for 16 h at rt. Saturated NH₄Cl(aq) (5 mL) was added and the solvent removed in vacuo. The residue was extracted with Et₂O (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Chromatography (petrol/ethyl acetate 9:1) gave 3c as a colorless oil (200 mg, 48%). ¹H NMR (400 MHz, CDCl₃) δ: 7.53 (d, J = 1.8, 2H, H₆), 7.38 (t, J = 1.8, 1H, H₇), 2.68 (s, 1H, H₀), 2.37 (br. s, 1H, H₈), 1.81 (s, 3H, H₉), 1.35 (s, 18H, H₁₀). ¹³C NMR (101 MHz, CDCl₃) δ: 150.9, 144.3, 122.1, 119.2, 87.8, 73.0, 70.6, 35.2, 33.3, 31.6. HR-El-MS m/z = 258.19876 M⁺ (calc. for C₁₈H₂₆O₂ 258.19782).

Figure S9 ¹H NMR (CDCl₃, 400 MHz) of 3c
Figure S10 | JMOD NMR (CDCl$_3$, 101 MHz) of 3c

1,3-Di-tert-butyl-5-(prop-2-yn-1-yl)benzene (3e)

S3 (200 mg, 0.86 mmol), dimethyl(1-diazo-2-oxo-propyl)phosphonate (192 mg, 1.00 mmol), and K$_2$CO$_3$ (235 mg, 1.7 mmol) were stirred in MeOH (2 mL) for 19 h at rt. The mixture was diluted with CH$_2$Cl$_2$ (10 mL), filtered and the filtrate washed with H$_2$O (5 mL) and brine (5 mL). The combined aqueous layers were extracted with CH$_2$Cl$_2$ (10 mL). The combined organic layers were dried (MgSO$_4$), filtered and the solvent removed in vacuo. Chromatography (petrol) gave 3e as a colorless oil (160 mg, 81%). $^1$H NMR (400 MHz, CDCl$_3$) δ: 7.31 (t, $J$ = 1.8, 1H, H$_B$), 7.20 (d, $J$ = 1.8, 2H, H$_C$), 3.60 (d, $J$ = 2.6, 2H, H$_D$), 2.18 (t, $J$ = 2.6, 1H, H$_E$), 1.33 (s, 18H, H$_A$). $^{13}$C NMR (101 MHz, CDCl$_3$) δ: 151.2, 135.2, 122.3, 120.9, 82.6, 70.4, 35.0, 31.6, 25.3. HR-El-MS $m/z$ = 228.18696 M$^+$ (calc. for C$_{17}$H$_{24}$ 228.18725).
Figure S11 $^1$H NMR (CDCl$_3$, 400 MHz) of 3e

Figure S12 $^{13}$C NMR (CDCl$_3$, 101 MHz) of 3e
1-(3,5-Di-tert-butylphenyl)but-3-yn-2-ol (3b)

**S3** (400 mg, 1.7 mmol) was dissolved in THF (3 mL) at 0 °C under N₂. Ethynylmagnesium bromide (0.5 M in THF, 2.0 mmol, 4.0 mL) was added dropwise. The reaction mixture was stirred for 20 h at rt. Saturated NH₄Cl(aq) (5 mL) was added and the solvent was removed *in vacuo*. Chromatography (petrol/Et₂O 95:5) gave **3b** as a colourless oil (160 mg, 36 %). ¹H NMR (400 MHz, CDCl₃) δ: 7.33 (t, J = 1.9, 1H, HA), 7.13 (d, J = 1.9, 2H, H₂), 4.58 (app. qd, J = 6.1, 2.0, 1H, H₃), 3.03 (qd, J = 16.3, 6.5, 2H, H₄), 2.50 (d, J = 2.1, 1H, H₅), 1.88 (d, J = 6.1, 1H, H₆), 1.33 (s, 18H, H₇, H₈). ¹³C NMR (101 MHz, CDCl₃) δ: 151.0, 135.1, 124.2, 121.2, 84.6, 73.7, 63.2, 44.6, 34.9, 31.6. HR-El-MS m/z = 258.19765 M⁺ (calc. for C₁₈H₂₆O 258.19782).

![Figure S13](image-url) ¹H NMR (CDCl₃, 400 MHz) of 3b
Figure S14 $^{13}$C NMR (CDCl$_3$, 101 MHz) of 3b
3. **Synthesis of acrylamide rotaxanes**

**General Procedure A**

KF\(_{aq}\) (0.1 M, 0.8 eq.) was added to a solution of alkyn (1.2 eq.), azide (1.2 eq.), macrocycle (1 eq.) and [Cu(MeCN)]\(_4\)PF\(_6\) (0.96 eq.) in THF (72 mL/mmol) in a microwave vial (CEM Ltd.) and the vial sealed. The orange mixture was stirred at 70 °C under microwave irradiation for 1 hour. The reaction mixture was diluted with CH\(_2\)Cl\(_2\) (200 mL/mmol), washed with EDTA-NH\(_3\) solution (100 mL/mmol). The aqueous layer was extracted with CH\(_2\)Cl\(_2\) (2 × 100 mL/mmol). The combined organic extracts were washed with brine (100 mL/mmol), dried (MgSO\(_4\)), filtered and the solvent removed *in vacuo*.

**Rotaxane 5**

Prepared according to *general procedure A* with 1a (24.0 mg, 0.05 mmol), [Cu(MeCN)]\(_4\)PF\(_6\) (17.9 mg, 0.048 mmol), 2a (13.8 mg, 0.06 mmol), and 3a (14.6 mg, 0.06 mmol). Chromatography (petrol with a gradient of 0 to 20% Et\(_2\)O) gave 5 as a white foam (44.0 mg, 95%). \(^1\)H NMR (500 MHz, CDCl\(_3\) \(\delta\): 9.91 (S, 1H, H\(_f\)), 7.65 (t, \(J=7.8, 2H, H_b\)), 7.49 (dd, \(J=7.8, 1.0, 2H, H_a\)), 7.23 (t, \(J=1.8, 1H, H_i\)), 7.14 – 7.10 (m, 4H, H\(_g\)), 6.94 – 6.92 (m, 3H, H\(_h\)), 6.85 (d, \(J=15.5, 1H, H_j\)), 6.69 (s, 8H, H\(_b\), H\(_n\)), 6.29 (d, \(J=15.5, 1H, H_j\)), 4.70 - 4.55 (m, 2H, H\(_i\)), 4.21 - 4.10 (m, 2H, H\(_l\)), 2.62 - 2.42 (m, 8H, H\(_b\), H\(_n\)), 2.40 - 2.30 (m, 2H, H\(_j\)), 2.11 – 2.00 (m, 2H, H\(_i\)), 1.88 – 1.64 (m, 4H, H\(_g\)), 1.23 (s, 18H, H\(_a\)), 1.17 (s, 18H, H\(_i\)). \(^{13}\)C NMR (126 MHz, CDCl\(_3\) \(\delta\): 163.8, 163.5, 157.4, 156.8, 150.3, 150.1, 139.6, 139.0, 137.0, 135.9, 132.4, 129.1, 123.3, 122.2, 122.0, 121.8, 119.6, 116.2, 116.2, 115.0, 114.2, 66.3, 36.6, 35.2, 34.8, 34.8, 31.5, 31.5, 31.3, 25.0. HR-ESI-MS \(m/z = 926.6199 \quad [M+H]^+\) (calc. for C\(_{63}\)H\(_{80}\)N\(_3\)O\(_3\) 926.6194).
Figure S15 Stacked partial $^1$H NMR (400 MHz, CDCl$_3$) spectra of 5 (top), 4 (middle) and the crude reaction product before chromatography (bottom). Ratio of 5 : 4 = 100:0.

Figure S16 $^1$H NMR (CDCl$_3$, 500 MHz) of 5
Figure S17 JMOD NMR (CDCl$_3$, 126 MHz) of 5

Figure S18 COSY NMR (CDCl$_3$) of 5
Figure S19 HSQC NMR (CDCl₃) of 5

Figure S20 HMBC NMR (CDCl₃) of 5
Rotaxane 6

Prepared according to general procedure A with 1b (48.3 mg, 0.1 mmol), [Cu(MeCN)₄]PF₆ (35.8 mg, 0.096 mmol), 2a (29.3 mg, 0.12 mmol), 3a (27.8 mg, 0.12 mmol). Chromatography (petrol with a gradient of 0 to 20% Et₂O) gave 6 as a white foam (90.0 mg, 97%). ¹H NMR (400 MHz, CDCl₃) δ: 9.94 (s, 1H, Hf), 7.77 (t, J = 7.7, 2H, Hb), 7.67 (dd, J = 7.7, 1.0, 2H, Ha), 7.50 (dd, J = 7.7, 1.0, 2H, Hc), 7.27 (d, J = 1.8, 2H, Hg), 7.23 (t, J = 1.8, 1H, Ha), 6.98 (t, J = 1.8, 1H, Hb), 6.91 (d, J = 8.5, 4H, Hf), 6.81 (d, J = 16.0, 1H, Hj), 6.79 (d, J = 1.8, 2H, Hc), 6.70 (d, J = 8.5, 4H, Hg), 5.92 (d, J = 16.0, 1H, Hk), 4.77 – 4.70 (m, 2H, 2 of Hi), 4.69 (d, J = 12.0, 2H, 2 of Ho), 4.33 (d, J = 12.0, 2H, 2 of Ho), 4.19 (d, J = 13.8, 2H, 2 of Hc), 4.18 – 4.12 (m, 2H, 2 of Hi), 4.02 (d, J = 13.8, 2H, 2 of Hj), 2.46 – 2.33 (m, 2H, 2 of Hf), 1.11 (s, 1H, Hf or Hb), 1.19 (s 18H, H or Hb). ¹³C NMR (101 MHz, CDCl₃) δ: 163.3, 160.1, 159.2, 154.9, 150.5, 150.3, 139.6, 139.4, 127.5, 135.6, 129.9, 128.2, 122.9, 122.3, 122.1, 120.8, 119.9, 116.4, 115.1, 114.1, 72.9, 69.5, 66.1, 34.9, 34.8, 31.5, 25.0, 24.8. HR-ESI-MS m/z = 930.5763 [M+H]⁺ (calc. for C₃₇H₇₆N₄O₉ 930.5779).

Figure S21 Stacked partial ¹H NMR (400 MHz, CDCl₃) spectra of S4 (top), 6 (middle), the crude reaction product before chromatography (bottom). Ratio of 6 : S4 = 100 : 0.
Figure S22 $^1$H NMR (CDCl$_3$, 400 MHz) of 6

Figure S23 JMOD NMR (CDCl$_3$, 101 MHz) of 6
Figure S24 COSY NMR (CDCl₃) of 6

Figure S25 HSQC NMR (CDCl₃) of 6
Figure S26 HMBC NMR (CDCl$_3$) of 6
Rotaxane 7

Prepared according to modified general procedure A (T = 150 °C, t = 2 h) with 1d (12.5 mg, 0.025 mmol), [Cu(MeCN)]PF₆ (8.9 mg, 0.024 mmol), 2a (6.9 mg, 0.03 mmol), and 3a (7.3 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 50% Et₂O) gave 7 as a white foam (11.8 mg, 50%). ¹H NMR (500 MHz, CDCl₃) δ: 9.78 (s, 1H, Hf), 7.90 (t, J = 7.8, 2H, Ha), 7.80 (dd, J = 7.8, 0.9, 2H, Hb), 7.57 (dd, J = 7.8, 0.9, 2H, Hc), 7.42 (d, J = 8.5, 4H, Hd), 7.30 (t, J = 1.8, 1H, He), 7.27 (d, J = 16.0, Hd), 7.06 (d, J = 1.8, 2H, Hc), 6.90 (apps, 3H, Hp, Hb), 6.63 (d, J = 8.5, 4H, He), 6.46 (d, J = 16.0, 1H, Hc), 4.26 – 4.14 (m, 4H, Hf), 3.96 – 3.64 (m, 12H, Hi, Hj, Hk), 1.33 (s, 18H, Ha), 1.12 (s, 18H, Hb). ¹³C NMR (126 MHz, CDCl₃) δ: 163.6, 159.9, 158.9, 157.2, 150.6, 150.2, 138.7, 138.5, 137.7, 135.5, 132.4, 129.4, 124.3, 122.8, 122.1, 120.5, 119.6, 116.7, 115.1, 113.6, 70.3, 70.1, 68.3, 66.9, 34.9, 34.7, 31.5 (×2). HR-ESI-MS m/z = 946.5712 [M+H]+ (calc. for C₆₁H₇₆N₃O₉ 946.5729).

Figure S27 Stacked partial ¹H NMR (400 MHz, CDCl₃) spectra of S5 (top), 7 (upper middle), macrocycle 1d (lower middle) and the crude reaction product before chromatography (bottom). Ratio of 7 : oxidised product of S5 = 80 : 20 (under these conditions the triazole derived rotaxane was observed to spontaneously oxidise to the ketone).
Figure S28: $^1$H NMR (CDCl$_3$, 500 MHz) of 7

Figure S29: $^{13}$C NMR (CDCl$_3$, 126 MHz) of 7
Figure S30 COSY NMR (CDCl₃) of 7

Figure S31 HSQC NMR (CDCl₃) of 7
Figure S32 HMBC NMR (CDCl₃) of 7
Rotaxane 8

Prepared according to **general procedure A** with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)]PF₆ (8.9 mg, 0.024 mmol), 2b (7.3 mg, 0.03 mmol), and 3a (7.3 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 20% Et₂O) gave 8 as a white foam (16.0 mg, 68 %). ¹H NMR (500 MHz, CDCl₃) δ: 8.77 (t, J = 4.8, 1H, H_f), 7.60 (t, J = 7.8, 2H, H_B), 7.44 (dd, J = 7.8, 1.0, 2H, H_A), 7.21 (t, J = 1.8, 1H, H_a), 7.19 (d, J = 16.0, 1H, H_d), 7.07 (dd, J = 7.8, 1.0, 2H, H_c), 7.04 (j, J = 1.9, 1H, H_i), 6.88 (d, J = 1.9, 2H, H_h), 6.79 (s, 8H, H_G, H_H), 6.77 (d, J = 1.8, 2H, H_e), 6.35 (d, J = 16.0, 1H, H_d), 4.33 – 4.23 (m, 4H, H_i), 3.41 (d, J = 4.8, 2H, H_g), 2.61 – 2.47 (m, 4H, H_h), 2.46 – 2.34 (m, 4H, H_d), 2.17 – 2.10 (m, 4H, H_c), 1.83 – 1.70 (m, 4H, H_b), 1.16 (s, 18H, H_a), 1.06 (s, 18H, H_j). ¹³C NMR (126 MHz, CDCl₃) δ: 165.4, 163.6, 157.3, 156.5, 150.4, 149.8, 137.6, 137.2, 136.9, 135.7, 132.6, 129.4, 123.2, 122.9, 122.3, 121.9, 121.9, 120.5, 119.5, 115.2, 66.6, 44.2, 36.5, 35.2, 34.8, 34.7, 31.5, 31.4, 31.4, 25.0; HR-ESI-MS m/z = 940.6351 [M+H]+ (calc. for C₆₄H₈₂N₃O₉ 940.6351).

**Figure S33** Stacked partial ¹H NMR (400 MHz, CDCl₃) spectra of 8 (top), S6 (middle) and the crude reaction product before chromatography (bottom). Ratio of 8 : S6 = 75 : 25.
Figure S34 $^1$H NMR (CDCl$_3$, 500 MHz) of 8

Figure S35 JMOD NMR (CDCl$_3$, 126 MHz) of 8
Figure S36 COSY NMR (CDCl₃) of 8

Figure S37 HSQC NMR (CDCl₃) of 8
Figure S38 HMBC NMR (CDCl₃) of 8
Rotaxane 9

Prepared according to general procedure A with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)]PF₆ (8.9 mg, 0.024 mmol), 2c (9.1 mg, 0.03 mmol), and 3a (7.3 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 50% Et₂O) gave 9 as a colourless oil (4.0 mg, 16%). ¹H NMR (500 MHz, CDCl₃) δ: 8.43 (t, J = 5.4, 1H, Hf), 7.65 (t, J = 7.8, 2H, Hb), 7.48 (dd, J = 7.8, 0.9, 2H, Ha), 7.31 (t, J = 1.9, 1H, Hj), 7.27 (d, J = 16.0, 1H, Hd), 7.23 (t, J = 1.9, 1H, Hg), 7.18 (dd, J = 7.8, 0.9, 2H, Hc), 7.02 (d, J = 1.9, 2H, Hl), 6.92 (d, J = 1.9, 2H, Hk), 6.90 (d, J = 8.5, 4H, Hc), 6.82 (d, J = 8.5, 4H, Hj), 6.32 (d, J = 16.0, 1H, Hj), 4.29 – 4.13 (m, 4H, Hg), 4.08 (s, 2H, Hb), 3.02 (t, J = 7.2, 2H, Hf), 2.70 – 2.53 (m, 8H, Hb, Hg), 2.29 – 2.23 (m, 2H, Hc), 2.18 – 1.99 (m, 4H, Hk), 1.97 – 1.75 (m, 4H, Hg), 1.30 (s, 18H, Hm), 0.97 (t, J = 7.8, 2H, Hf). ¹³C NMR (126 MHz, CDCl₃) δ: 165.4, 163.5, 157.5, 156.6, 150.7, 150.6, 137.9, 137.8, 137.1, 135.5, 132.8, 129.6, 123.2, 122.6, 122.1, 121.9, 121.7, 119.8, 115.1, 73.5, 68.8, 66.5, 36.6, 35.5, 35.3, 34.9, 34.8, 31.6, 31.5, 31.4, 28.8, 25.0. HR-ESI-MS m/z = 998.6749 [M+H]+ (calc. for C₆₄H₈₂N₃O₉ 998.6769).

Figure S39 Stacked partial ¹H NMR (400 MHz, CDCl₃) spectra of S7 (top), 9 (middle) and the crude reaction product before chromatography (bottom). Ratio of 9 : S7 = 35 : 65.
Figure S40 $^1$H NMR (CDCl$_3$, 500 MHz) of 9

Figure S41 JMOD NMR (CDCl$_3$, 126 MHz) of 9
Figure S42 COSY NMR (CDCl₃) of 9

Figure S43 HSQC NMR (CDCl₃) of 9
Figure S44 HMBC NMR (CDCl₃) of 9
Rotaxane 10

Prepared according to **general procedure A** with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)₄]PF₆ (8.9 mg, 0.024 mmol), 2a (6.9 mg, 0.03 mmol), and 3b (7.8 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 20% Et₂O) gave 10 as a colourless oil (10.0 mg, 43%). ¹H NMR (400 MHz, CDCl₃) δ: 9.92 (s, 1H, H₉), 7.62 (t, J=7.9, 2H, H₈), 7.48 (dd, J=7.9, 0.9, 2H, H₇), 7.15 (t, J=1.9, 1H, H₆), 7.10 (dd, J=7.9, 0.9, 2H, H₅), 6.97 (d, J=1.9, 2H, H₄), 6.85 (t, J=1.9, 1H, H₃), 6.82 (d, J=1.9, 2H, H₂), 6.77 (d, J=8.5, 4H, H₁), 6.70 (d, J=8.5, 4H, H₁₀), 6.42 (dt, J=15.5, 6.8, 1H, H₁₁), 5.46 (dt, J=15.5, 1.6, 1H, H₁₂), 4.50 – 4.38 (m, 2H, 2 of H₁₃), 4.17 – 4.06 (m, 2H, 2 of H₁₄), 2.93 (d, J=6.8, 2H, H₁₅), 2.63 – 2.41 (m, 8H, H₁₆, H₁₇), 2.29 – 2.16 (m, 2H, 2 of H₁₈), 2.07 – 1.95 (m, 2H, 2 of H₁₉), 1.90 – 1.67 (m, 4H, H₂₀), 1.21 (s, 18H, H₂₁ or H₂₂). ¹³C NMR (101 MHz, CDCl₃) δ: 163.6, 163.3, 157.6, 156.3, 150.4, 150.0, 141.3, 139.4, 138.5, 137.0, 132.6, 129.2, 125.6, 122.9, 121.9, 120.2, 119.6, 116.0, 115.1, 114.3, 66.5, 39.4, 36.6, 35.2, 34.8 (×2), 31.6, 31.5, 31.1, 25.2. HR-ESI-MS m/z = 940.6367 [M+H]⁺ (calc. for C₆₄H₈₂N₃O₉ 940.6351).

**Figure S45** Stacked partial ¹H NMR (400 MHz, CDCl₃) spectra of 10 (top), S8 (middle) and the crude reaction product before chromatography (bottom). Ratio of 10 : S8 = 60 : 40.
Figure S46 $^1$H NMR (CDCl$_3$, 400 MHz) of 10

Figure S47 $^1$JMOD NMR (CDCl$_3$, 101 MHz) of 10
Figure S48 COSY NMR (CDCl$_3$) of 10

Figure S49 HSQC NMR (CDCl$_3$) of 10
Figure S50 HMBC NMR (CDCl₃) of 10
Rotaxane 11

Prepared according to general procedure A with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)]_4PF_6 (8.9 mg, 0.024 mmol), 2a (6.9 mg, 0.03 mmol), and 3c (7.7 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 30% Et_2O) gave 11 as a colourless oil (19.9 mg, 85%). \(^1\)H NMR (500 MHz, CDCl_3) \(\delta\): 10.29 (s, 1H, H_f), 7.66 (t, \(J = 7.8\), 2H, H_B), 7.55 (dd, \(J = 7.8, 0.9\), 2H, H_a), 7.24 (d, \(J = 1.9\), 2H, H_e), 7.17 (t, \(J = 1.9\), 1H, H_b), 7.13 (dd, \(J = 7.8, 0.9\), 2H, H_c), 7.05 (d, \(J = 1.9\), 2H, H_d), 6.93 (t, \(J = 1.9\), 1H, H_h), 7.74 (d, \(J = 8.5\), 4H, H_g), 6.61 (d, \(J = 8.5\), 4H, H_i), 6.54 (q, \(J = 1.2\), 1H, H_d), 4.72 - 4.64 (m, 2H, 2 of H_I), 4.21 - 4.15 (m, 2H, 2 of H_I), 2.59 - 2.43 (m, 8H, H_D, H_F), 2.35 - 2.25 (m, 2H, 2 of H_h), 2.12 (d, \(J = 1.2\), 3H, Hd), 2.09 - 1.98 (m, 2H, 2 of H_d), 1.82 - 1.60 (m, 4H, H_e), 1.19 (s, 18H, H_a), 1.08 (s, 18H, H_c). \(^{13}\)C NMR (126 MHz, CDCl_3) \(\delta\): 164.0, 163.2, 157.7, 156.5, 150.0, 149.9, 147.5, 142.8, 140.6, 137.0, 132.1, 128.9, 122.2, 122.1, 121.3, 120.5, 119.4, 115.3, 115.2, 113.3, 66.4, 36.8, 35.4, 34.9, 34.8, 31.6, 31.4, 25.0, 17.0. HR-ESI-MS m/z = 940.6343 [M+H]^+ (calc. for C_{64}H_{82}N_3O_3 940.6351).

**Figure S51** Stacked partial \(^1\)H NMR (400 MHz, CDCl_3) spectra of S9 (top), 11 (middle) and the crude reaction product before chromatography (bottom). Ratio of 11 : S9 = 95 : 5.
Figure S52 $^1$H NMR (CDCl$_3$, 500 MHz) of 11

Figure S53 JMOD NMR (CDCl$_3$, 126 MHz) of 11
Figure S54 COSY NMR (CDCl$_3$) of 11

Figure S55 HSQC NMR (CDCl$_3$) of 11
Figure S56 HMBC NMR (CDCl₃) of 11
4. Synthesis of triazole rotaxanes

General Procedure B

NPPr$_2$Et (2 eq.) was added to a solution of alkyne (1.2 eq.), azide (1.2 eq.), macrocycle (1 eq.) and [Cu(MeCN)$_4$]PF$_6$ (0.96 eq.) in CH$_2$Cl$_2$ (80 mL/mmol) in a sealed microwave vial (CEM Ltd.). The deep red mixture was stirred at rt for 16 hours. The reaction mixture was diluted with CH$_2$Cl$_2$ (20 mL/mmol) and washed with EDTA-NH$_3$ solution (100 mL/mmol). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 x 100 mL). Combined organic extracts were washed with brine (100 mL/mmol), dried (MgSO$_4$), filtered and the solvent removed *in vacuo.*

Rotaxane 4

Prepared according to general procedure B with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)$_4$]PF$_6$ (8.9 mg, 0.024 mmol), 2a (7.0 mg, 0.03 mmol), and 3a (7.3 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 50% Et$_2$O) gave 4 as a white foam (18.0 mg, 76%). $^1$H NMR (500 MHz, CDCl$_3$): δ 10.08 (d, $J$ = 0.8, 1H, H$_f$), 7.73 (t, $J$ = 7.8 1H, 1 of H$_B$), 7.69 (t, $J$ = 7.8, 1H, 1 of H$_B$), 7.53 (dd, $J$ = 7.8, 1.0, 1H, 1 of H$_A$), 7.50 (dd, $J$ = 7.8, 1.0, 1H, 1 of H$_A$), 7.44 (dd, $J$ = 1.9, 0.6, 2H, H$_c$), 7.41 (d, $J$ = 1.9, 2H, H$_c$), 7.18 – 7.21 (m, 2H, 1 of H$_C$, H$_H$), 7.13 (dd, $J$ = 7.8, 0.8, 1H, 1 of H$_C$), 6.63 (d, $J$ = 8.6, 2H, 1 of H$_A$), 6.51 (d, $J$ = 8.6, 2H, 1 of H$_A$), 6.05 – 6.11 (m, 4H, 1 of H$_C$, 1 of H$_H$), 5.66 (br s, 1H, H$_d$), 4.64 – 4.77 (m, 1H, 1 of H$_j$), 4.49 – 4.60 (m, 1H, 1 of H$_j$), 4.41 (s, 1H, H$_e$), 4.21 – 4.30 (m, 1H, 1 of H$_i$), 3.91 – 4.00 (m, 1H, 1 of H$_i$), 2.12 – 2.60 (m, 10H, H$_b$, 2 of H$_b$, H$_d$), 1.96 – 2.07 (m, 2H, 2 of H$_j$), 1.53 – 1.79 (m, 4H, H$_e$), 1.32 (s, 18H, H$_a$), 1.19 (s, 18H, H$_i$). $^{13}$C NMR (126 MHz, CDCl$_3$): δ 163.4, 163.1, 157.9, 157.1, 155.3, 156.9, 151.1, 150.0, 149.9, 142.6, 137.3, 137.1, 131.7, 151.7, 128.3, 128.2, 122.4, 121.6, 121.5, 121.4, 120.6, 120.2, 120.1, 120.1, 115.4, 114.4, 114.3, 69.9, 66.8, 66.3, 36.9, 36.1, 35.1, 35.0, 34.7, 32.3, 31.7, 31.4, 30.0, 25.1, 24.9. HR-ESI-MS m/z = 954.6257 [M+H]$^+$ (calc. for C$_{63}$H$_{80}$N$_5$O$_3$ 954.6256).
Figure S57 ¹H NMR (CDCl₃, 500 MHz) of 4

Figure S58 JMOD NMR (CDCl₃, 126 MHz) of 4
Figure S59 COSY NMR (CDCl₃) of 4

Figure S60 HSQC NMR (CDCl₃) of 4
Figure S61 HMBC NMR (CDCl₃) of 4
Rotaxane S4

Prepared according to **general procedure B** with 1b (48.3 mg, 0.1 mmol), [Cu(MeCN)]$_4$PF$_6$ (35.8 mg, 0.096 mmol), 2a (29.3 mg, 0.12 mmol), and 3a (27.8 mg, 0.12 mmol). Chromatography (petrol with a gradient of 0 to 50% Et$_2$O) gave S4 as a white foam (90.0 mg, 97%). $^1$H NMR (400 MHz, CDCl$_3$): δ 9.65 (s, 1H, H$_f$), 7.75 – 7.68 (m, 2H, H$_B$), 7.62 (dd, $J$=7.8, 1.0, 1H, 1 of H$_A$), 7.58 (dd, $J$=7.8, 1.0, 1H, 1 of H$_A$), 7.42 (dd, $J$=7.8, 1.0, 2H, H$_C$), 7.40 (d, $J$=1.9, 2H, H$_d$), 7.28 (t, $J$=1.9, 1H, H$_b$), 7.14 (d, $J$=1.9, 2H, H$_d$), 7.10 (t, $J$=1.9, 1H, H$_b$), 6.70 (d, $J$=8.5, 2H, 2 of H$_F$), 6.54 ($J$=8.5, 2H, 2 of H$_G$), 6.23 (d, $J$=8.5, 2H, 2 of H$_G$), 5.97 (d, $J$=8.5, 2H, 2 of H$_C$), 5.62 (s, 1H, H$_d$), 4.68 (q, $J$=7.8, 1H, 1 of H$_i$), 4.57 (d, $J$=12.2, 1H, 1 of H$_b$), 4.48 (q, $J$=7.8, 1H, 1 of H$_b$), 4.36 (d, $J$=12.2, 1H, 1 of H$_b$), 4.21 (d, $J$=12.2, 1H, 1 of H$_b$), 4.16 (q, $J$=7.8, 1H, 1 of H$_i$), 4.02 (t, $J$=12.2, 2H, 1 of H$_D$, 1 of H$_E$), 3.95 (q, $J$=12.2, 2H, 2 of H$_D$), 3.83 (q, $J$=7.8, 1H, 1 of H$_i$), 3.77 (d, $J$=12.2, 1H, H$_b$), 2.40 - 2.33 (m, 2H, 2 of H$_i$), 2.00 - 1.83 (m, 2H, 2 of H$_i$), 1.27 (s, 2H, H$_o$ or H$_i$), 1.09 (s, 2H, H$_o$ or H$_i$). $^{13}$C NMR (101 MHz, CDCl$_3$): δ 159.6, 159.6, 159.3, 158.6, 155.2, 155.1, 151.2, 147.9, 149.7, 142.3, 137.6, 137.4, 136.8, 129.4, 128.9, 127.9, 127.2, 121.8, 121.5, 120.9, 120.7, 120.4, 120.2, 120.2, 120.1, 115.3, 114.2, 114.0, 73.0, 72.9, 70.5, 70.0, 69.8, 66.7, 66.0, 34.9, 34.9, 31.6, 31.3, 24.8, 24.7. HR-ESI-MS $m/z$ = 958.5843 [M+H]$^+$ (calc. for C$_{61}$H$_{76}$N$_5$ 958.5841).

Figure S62 $^1$H NMR (CDCl$_3$, 400 MHz) of S4
Figure S63 JMOD NMR (CDCl$_3$, 101 MHz) of S4

Figure S64 COSY NMR (CDCl$_3$) of S4
Figure S65 HSQC NMR (CDCl₃) of S4

Figure S66 HMBC NMR (CDCl₃) of S4
Rotaxane S5

Prepared according to general procedure B with 1d (12.0 mg, 0.025 mmol), [Cu(MeCN)$_4$]PF$_6$ (8.9 mg, 0.024 mmol), 2a (6.9 mg, 0.03 mmol), and 3a (7.3 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 50% Et$_2$O) gave S5 as a white foam (9.0 mg, 37%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 9.91 (s, 1H, H$_f$), 7.93 (t, $J = 7.8$, 1H, 1 of H$_b$), 7.79 (dd, $J = 7.8$, 0.9, 1H, 1 of H$_c$), 7.77 (dd, $J = 7.8$, 0.9, 1H, 1 of H$_a$), 7.64 (dd, $J = 7.8$, 0.9, 1H 1 of H$_c$), 7.46 (dd, $J = 7.8$, 0.9, 1H, 1 of H$_a$), 7.41 (d, $J = 1.8$, 2H, H$_e$), 7.29 (d, $J = 8.7$, 2H, 2 of H$_c$), 7.21 (t, $J = 1.8$, 1H, H$_b$), 7.15 (t, $J = 1.8$, 1H, H$_b$), 7.11 (d, $J = 1.8$, 2H, H$_c$), 6.86 (d, $J = 8.7$, 2H, 2 of H$_c$), 6.35 (d, $J = 8.7$, 2H, 2 of H$_b$), 6.07 (d, $J = 8.7$, 2H, 2 of H$_b$), 5.00 (d, $J = 2.3$, 1H, H$_d$), 4.07 - 3.51 (m, 16H, H$_F$, H$_G$, H$_H$, H$_I$), 2.99 (d, $J = 2.3$, 1H, H$_d$), 1.12 (s, 18H, H$_i$), 1.09 (s, 18H, H$_i$). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$: 160.07, 159.47, 159.12, 158.45, 157.67, 157.40, 151.48, 150.44, 149.46, 142.21, 137.60, 137.53, 136.71, 132.80, 132.08, 129.54, 129.13, 125.67, 123.99, 121.90, 121.64, 120.64, 120.35, 120.15, 119.93, 119.62, 114.67, 114.33, 114.15, 70.14, 70.01, 69.91, 69.79, 69.64, 68.85, 68.22, 67.17, 66.09, 34.98, 34.79, 31.47, 31.33. HR-ESI-MS $m/z$ = 974.5783 [M+H]$^+$ (calc. for C$_{61}$H$_{76}$N$_5$O$_6$ 974.5790).

Figure S67 $^1$H NMR (CDCl$_3$, 500 MHz) of S5
Figure S68 JMOD NMR (CDCl₃, 126 MHz) of S5

Figure S69 COSY NMR (CDCl₃) of S5
Figure S70 HSQC NMR (CDCl₃) of S5

Figure S71 HMBC NMR (CDCl₃) of S5
Rotaxane S6

Prepared according to **general procedure B** with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)_{4}]PF_{6} (8.9 mg, 0.024 mmol), 2b (7.3 mg, 0.03 mmol), and 3a (7.3 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 50% Et_{2}O) gave S6 as a white foam (17.0 mg, 70%).

^{1}H NMR (400 MHz, CDCl_{3}): δ 8.73 (s, 1H, H_{f}), 7.62 (t, J = 7.8, 2H, H_{b}), 7.26 (app. s, 3H, H_{a} H_{b} H_{c}), 7.16 (t, J = 1.8, 1H, H_{i}), 7.10 (app. t, J = 7.7, 2H, H_{c}) 6.79 (d, J = 1.8, 2H, H_{b}), 6.68 – 6.57 (m, 4H, 2 of H_{a} 2 of H_{b}), 6.48 (s, 4H, 2 of H_{a} 2 of H_{b}), 5.38 (br. s, 1H, H_{d}), 4.67 (d, J = 3.7, 1H, H_{e}), 4.65 – 4.52 (m, 2H, 2 of H_{i}), 4.49 (d, J = 13.9, 1H, 1 of H_{g}), 4.25 (d, J = 13.9, 1H, 1 of H_{g}), 4.18 – 4.00 (m, 2H, 2 of H_{i}), 2.68 – 2.15 (m, 10H, H_{b} H_{e} 2 of H_{i}), 2.03 – 1.95 (m, 2H, 2 of H_{i}), 1.85 – 1.49 (m, 4H, H_{c}), 1.26 (s, 18H, H_{a} or H_{b}), 1.11 (s, 18H, H_{a} or H_{b}).

^{13}C NMR (101 MHz, CDCl_{3}): δ 162.8, 162.8, 157.6, 157.4, 156.9, 156.7, 150.7, 149.9, 149.2, 142.4, 137.1, 136.9, 133.2, 132.4, 132.3, 128.9, 128.7, 124.2, 123.3, 122.8, 121.7, 121.6, 121.5, 120.7, 120.0, 119.9, 115.2, 114.9, 69.8, 66.7, 66.5, 53.4, 36.6, 36.3, 34.9, 34.9, 34.7, 34.7, 31.7, 31.5, 31.1, 30.5, 25.1, 25.0. HR-ESI-MS m/z = 968.6402 [M+H]^+ (calc. for C_{64}H_{102}N_{5}O_{3} 968.6412)

**Figure S72** ^{1}H NMR (CDCl_{3}, 400 MHz) of S6
Figure S73 JMOD NMR (CDCl₃, 101 MHz) of S6

Figure S74 COSY NMR (CDCl₃) of S6
Figure S75 HSQC NMR (CDCl$_3$) of S6

Figure S76 HMBC NMR (CDCl$_3$) of S6
Rotaxane S7

Prepared according to **general procedure B** with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)]$_4$PF$_6$ (8.9 mg, 0.024 mmol), 2c (9.1 mg, 0.03 mmol), and 3a (7.3 mg, 0.03 mmol). After purification by column chromatography on silica (petrol with a gradient of 0 to 50% Et$_2$O) S7 was obtained as a white foam (20.0 mg, 77%).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.32 (s, 1H, H$_f$), 7.63 (td, $J$ = 7.8, 2.6, 2H, H$_b$), 7.51 (d, $J$ = 7.7, 2H, H$_A$), 7.32 (t, $J$ = 1.9, 1H, H$_l$), 7.29 (t, $J$ = 1.9, 1H, H$_b$), 7.24 (t, $J$ = 1.9, 2H, H$_c$), 7.12 (d, $J$ = 7.7, H$_C$), 7.03 (d, $J$ = 1.9, 2H, H$_k$), 6.68 – 6.57 (m, 8H, H$_G$, H$_H$), 5.74 (d, $J$ = 4.5, 1H, H$_d$), 4.42 – 4.30 (m, 2H, 2 of H$_I$), 4.04 (s, 2H, H$_j$), 4.02 – 3.94 (m, 2H, 2 of H$_I$), 3.24 (d, $J$ = 4.7, 1H, H$_e$), 2.89 (t, $J$ = 6.7, 2H, H$_i$), 2.63 – 2.51 (m, 2H, H$_g$), 2.21 – 2.03 (m, 2H, 2 of H$_l$), 1.99 – 1.84 (m, 2H, 2 of H$_l$), 1.77 – 1.64 (m, 4H, H$_i$), 1.31 (s, 18H, Ha or Hm), 1.23 (s, 18H, H$_a$ or H$_m$), 1.04 – 0.88 (m, 2H, H$_h$). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 162.8, 162.8, 157.6, 157.6, 157.5 ($\times$2), 150.7, 150.7, 149.8, 142.2, 137.9, 137.0, 136.9, 133.0, 129.4 ($\times$2), 123.0, 122.0, 122.0, 121.7, 121.6, 121.6, 120.4, 120.4, 115.1, 115.0, 73.0, 70.4, 67.6, 66.5 ($\times$2), 46.7, 37.0 ($\times$2), 36.8 ($\times$2), 34.9, 34.9, 31.8, 31.7, 31.6, 28.8, 24.9, 24.9 ($\times$2). LR-ESI-MS m/z = 1026.68 [M+H]$^+$ (calc. for C$_{67}$H$_{88}$N$_5$O$_4$ 1026.68).

**Figure S77** Observed (top) and calculated (bottom) isotopic patterns for [M+H]$^+$ of S7
Figure S78 $^1$H NMR (CDCl$_3$, 400 MHz) of S7

Figure S79 JMOD NMR (CDCl$_3$, 101 MHz) of S7
Figure S80 COSY NMR (CDCl₃) of S7

Figure S81 HSQC NMR (CDCl₃) of S7
Figure S82 HMBC NMR (CDCl₃) of S7
Rotaxane S8

Prepared according to general procedure B with 1a (19.1 mg, 0.04 mmol), [Cu(MeCN)]₄PF₆ (14.1 mg, 0.038 mmol), 2a (10.4 mg, 0.045 mmol), and 3b (11.6 mg, 0.045 mmol). Chromatography (petrol with a gradient of 0 to 30% Et₂O) gave S8 as a white foam (31.0 mg, 80%). ^1H NMR (400 MHz, CDCl₃) δ: 10.13 (s, 1H, Hg), 7.66 (t, J = 7.8, 2H, Hb), 7.51 (d, J = 1.9, 2H, Hc), 7.44 (td, J = 8.0, 0.9, 2H, Ha), 7.29 (t, J = 1.9, 1H, Ha), 7.21 (t, J = 1.9, 1H, Hb), 6.95 (d, J = 1.9, 2H, Hc), 6.70 (s, 4H, 2 of Hg, 2 of Hii), 6.58 – 6.48 (m, 4H, 2 of Hg, 2 of Hii), 4.63 – 4.23 (m, 5H, Hb, Hc), 3.78 (s, 1H, Hf), 2.70 – 2.63 (m, 1H, 1 of Hf), 2.63 – 2.26 (m, 8H, Hb, Hf), 2.26 – 2.10 (m, 4H, Hf), 1.98 (dd, J = 14.6, 11.2, 1H, 1 of Hf), 1.90 – 1.64 (m, 4H, Hb), 1.32 (s, 18H, Hc), 1.21 (s, 18H, Hb). ^13C NMR (101 MHz, CDCl₃) δ 163.4, 163.4, 157.7, 157.7, 157.1, 157.1, 151.9, 149.8 (×2), 138.7 (×2), 137.4, 137.2, 137.1, 132.1, 128.8, 128.7, 123.7, 122.7, 122.0, 122.0, 121.0, 120.1, 120.0, 119.9, 115.4, 114.8, 114.4, 66.6, 66.6, 66.5, 43.6, 36.8 (×2), 35.4, 35.4, 35.2, 34.9, 32.0, 31.8, 31.4, 31.3, 25.1, 24.9. HR-ESI-MS m/z = 968.6392 [M+H]⁺ (calc. for C₆₄H₇₀N₅O₉ 968.6412).

Figure S83 ^1H NMR (CDCl₃, 400 MHz) of S8
Figure S84 JMOD NMR (CDCl₃, 101 MHz) of S8

Figure S85 COSY NMR (CDCl₃) of S8
Figure S86 HSQC NMR (CDCl₃) of S8

Figure S87 HMBC NMR (CDCl₃) of S8
\( \text{Pr}_2\text{NEt} \) (9.0 µl, 0.05 mmol) was added to a solution of 3c (6.5 mg, 0.025 mmol), 2a (5.8 mg, 0.025 mmol), 1a (12.0 mg, 0.025 mmol) and \([\text{Cu(MeCN)}_4]\)PF\(_6\) (8.9 mg, 0.024 mmol) in CH\(_2\)Cl\(_2\) (2.0 mL) in a microwave vial. The deep red mixture was stirred at rt for 16 h. TBACN (26.0 mg, 0.097 mmol) in CH\(_2\)Cl\(_2\) was added to the mixture and stirred for five days at rt until the solution turned black. N\(_2\) was bubbled through the reaction mixture to remove the solvent. The residue was diluted with CH\(_2\)Cl\(_2\) (20 mL), and washed with H\(_2\)O (10 mL). The aqueous layer was extracted with CH\(_2\)Cl\(_2\) (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO\(_4\)), filtered and the solvent removed in vacuo.

Chromatography (petrol:CH\(_2\)Cl\(_2\) 1:1, with a gradient of 0 to 5% acetonitrile) gave S9 as a white foam (20.0 mg, 84%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ: 10.06 (s, 1H, H\(_f\)), 7.72 (app t, \(J = 7.8\) 1H, 1 of H\(_g\)), 7.68 (app t, \(J = 7.7\) 1H, one of H\(_a\)), 7.56 (d, \(J = 1.8\) 2H, H\(_c\)), 7.52 (dd, \(J = 7.8, 0.9\) 1H, one of H\(_b\)), 7.50 – 7.46 (m, 3H, H\(_e\), one of H\(_a\)), 7.30 (t, \(J = 1.8\) 1H, H\(_b\)), 7.18-7.10 (m, 3H, H\(_h\), H\(_b\)), 6.48 (d, \(J = 8.6\) 2H, 2 of H\(_d\)), 6.27 (d, \(J = 8.6\) 2H, 2 of H\(_c\)), 6.20 (d, \(J = 8.6\) 2H, 2 of H\(_c\)), 6.01 (d, \(J = 8.6\) 2H, 2 of H\(_d\)). 4.81 (q, \(J = 7.9\) 1H, 1 of H\(_i\)), 4.66 (q, \(J = 7.9\) 1H, 1 of H\(_i\)), 4.19 – 4.10 (m, 1H, 1 of H\(_j\)), 4.03 – 3.81 (m, 2H, H\(_e\), 1 of H\(_g\)), 2.52 – 1.92 (m, 12H, H\(_{a\&b}\), H\(_f\), H\(_i\)), 1.70-1.50 (m, 7H, H\(_d\), H\(_e\)), 1.24 (s, 18H, H\(_a\)), 1.09 (s, 18H, H\(_i\)). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 163.4, 163.4, 157.5, 157.3, 156.9, 153.4, 150.9, 150.9, 149.7, 137.1, 137.1, 137.0, 131.6, 131.5, 128.2, 122.1, 121.8, 121.1, 120.7, 120.4, 120.2, 120.0, 129.4, 115.2, 113.6, 114.4, 72.3, 66.3, 66.3, 37.0, 36.8, 35.2, 35.1, 31.8, 31.5, 31.4, 31.0, 25.0, 24.3. HR-ESI-MS m/z =968.6397 [M+H]\(^+\) (calc. for C\(_{64}\)H\(_{82}\)N\(_5\)O\(_3\) 968.6412).

**Figure S88** \(^1\)H NMR (CDCl\(_3\), 400 MHz) of S9
Figure S89 $^{13}$C NMR (CDCl$_3$, 101 MHz) of S9

Figure S90 COSY NMR (CDCl$_3$) of S9
Figure S91 HSQC NMR (CDCl$_3$) of S9

Figure S92 HMBC NMR (CDCl$_3$) of S9
Rotaxane S10

Pr₂NEt (9.0 μL, 0.05 mmol) was added to a solution of 3d (6.5 mg, 0.025 mmol), 2a (5.8 mg, 0.025 mmol), 1a (12.0 mg, 0.025 mmol), and [Cu(MeCN)]₄PF₆ (8.9 mg, 0.024 mmol), in CH₂Cl₂ (2.0 mL) in a sealed microwave vial (CEM Ltd). The deep red mixture was stirred at rt for 16 h. KCN (10.0 mg, 0.153 mmol) in MeOH was added and the reaction mixture and stirred for two days at rt until the solution turned black. N₂ was bubbled through the reaction mixture to remove the solvent. The residue was diluted with CH₂Cl₂ (20 mL) and washed with H₂O (10 mL). The aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Chromatography (petrol with a gradient of 0 to 50% EtOAc) gave S10 as a white foam (4.7 mg, 19%). Decomposition to unidentified species was observed during purification, accounting for the low isolated yield. ¹H NMR (500 MHz, CDCl₃) δ: 10.24 (s, 1H, H₁), 7.73 (t, J = 7.8, 1H, 1 of H₂), 7.69 (t, J = 7.8, 1H, 1 of H₂), 7.60 (d, J = 1.7, 2H, H₂), 7.54 (ddd, J = 7.8, 2.7, 0.9, 2H, H₃), 7.25 (d, J = 2.7, 2H, H₄), 7.18 (t, J = 2.7, 1H, H₅), 7.12 (dd, J = 7.8, 1.0, 1H, 1 of H₆), 7.07 (dd, J = 7.8, 1.0, 1H, 1 of H₇), 6.44 (d, J = 8.6, 2H, 2 of H₈), 6.28 (d, J = 8.6, 2H, 2 of H₈), 6.18 (d, J = 8.6, 2H, 2 of H₈), 5.97 (d, J = 8.6, 2H, H₉), 4.91 (s, 1H, Hₐ), 4.89 – 4.81 (m, 1H, 1 of Hₐ), 4.81 – 4.73 (m, 1H, 1 of Hₐ), 4.19 – 4.11 (m, 1H, 1 of Hₐ), 4.10 – 4.06 (m, 1H, 1 of Hₐ), 3.00 (s, 3H, Hₐ), 2.48 – 1.95 (m, 2H, 2 of H₉), 2.36 – 2.25 (m, 14H, Hₐ, Hₐ, Hₐ, 2 of H₉), 1.17 (s, 36H, Hₐ, Hₐ). ¹³C NMR (126 MHz, CDCl₃) δ: 163.5, 163.5, 157.6, 157.5, 157.3, 157.1, 150.6, 150.4, 146.3, 141.0, 137.1, 137.0, 136.9, 131.5, 131.5, 128.2, 128.1, 124.2, 122.3, 121.9, 121.8, 121.0, 120.9, 119.9, 119.8, 115.21, 115.1, 114.9, 79.8, 66.7, 66.5, 56.7, 37.2, 37.0, 35.2, 35.2, 34.9, 31.9, 31.5, 31.5, 31.4, 24.9, 24.9. HR-ESI-MS m/z = 968.6402 [M+H]+ (calc. for C₆₈H₁₂₂N₃O₃ 968.6412).

Figure S93 ¹H NMR (CDCl₃, 500 MHz) of S10
Figure S94 $^{13}$C NMR (CDCl$_3$, 126 MHz) of S10

Figure S95 COSY NMR (CDCl$_3$) of S10
Figure S96 HSQC NMR (CDCl$_3$) of S10

Figure S97 HMBC NMR (CDCl$_3$) of S10
Rotaxane S11

Prepared according to general procedure B with 1a (12.0 mg, 0.025 mmol), [Cu(MeCN)]PF$_6$ (8.9 mg, 0.024 mmol), 2a (7.0 mg, 0.03 mmol), and 3e (7.0 mg, 0.03 mmol). Chromatography (petrol with a gradient of 0 to 40% Et$_2$O) gave S11 as a white foam (17.0 mg, 72%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 10.09 (s, 1H, H$_e$), 7.69 (t, $J$=7.7, 2H, H$_b$), 7.51 (dd, $J$=7.8, 0.9, 2H, H$_a$), 7.45 (d, $J$=1.7, 2H, H$_i$), 7.18 (t, $J$=1.7, 1H, H$_d$), 7.16 (t, $J$=1.7, 1H, H$_b$), 7.09 (dd, $J$=7.8, 0.9, 2H, H$_c$), 6.95 (d, $J$=1.8, 2H, H$_i$), 6.40 (d, $J$=8.5, 4H, H$_d$), 6.16 (d, $J$=8.5, 54H, H$_c$), 4.72 (q, $J$=7.8, 2H, H$_i$), 4.26-4.09 (m, 2H, H$_d$), 2.45 – 1.98 (m, 12H, H$_b$, H$_d$, H$_e$), 1.57 – 1.29 (m, 4H, H$_i$), 1.16 (s, 18H, H$_b$), 1.12 (s, 18H, H$_c$). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$: 163.5, 157.6, 157.3, 150.7, 150.5, 145.3, 139.6, 137.3, 136.9, 131.8, 128.2, 123.8, 123.1, 122.0, 120.8, 120.6, 119.7, 115.4, 115.1, 68.8, 37.0, 35.2, 35.1, 34.7, 33.2, 32.2, 31.5, 31.5, 25.0. HR-ESI-MS $m/z$ = 938.6307 [M+H]$^+$ (calc. for C$_{63}$H$_{80}$N$_5$O$_2$ 938.6307).

Figure S98 $^1$H NMR (CDCl$_3$, 400 MHz) of S11
Figure S99 JMOD NMR (CDCl$_3$, 101 MHz) of S11

Figure S100 COSY NMR (CDCl$_3$) of S11
Figure S101 HSQC NMR (CDCl₃) of S11

Figure S102 HMBC NMR (CDCl₃) of S11
2a (24.4 mg, 0.1 mmol), 3a (23.1 mg, 0.1 mmol), CuSO₄·5H₂O (12.5 mg, 0.05 mmol), and sodium ascorbate (19.8 mg, 0.1 mmol) were placed in a round bottom flask. DMF (2mL) was added and the mixture was stirred for 16 h. The crude reaction mixture was diluted with Et₂O (10 mL), washed with H₂O (2 × 10 mL), brine (5 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Chromatography (petrol with 0 to 50% Et₂O) gave S12 as a white foam (37.0 mg, 78%). ¹H NMR (400 MHz, CDCl₃): δ 7.74 (s, 1H, Hₑ), 7.48 (t, J = 1.7, 1H, Hₙ), 7.47 (d, J = 1.7, 2H, Hₙ), 7.40 (t, J = 1.7, 1H, Hₙ), 7.38 (d, J = 1.7, 2H, Hₙ), 6.11 (d, J = 3.7, 1H, Hₐ), 2.85 (d, J = 3.7, 1H, Hₐ), 1.35 (s, 18H, Hₐ), 1.33 (s, 18H, Hₐ). ¹³C NMR (101 MHz, CDCl₃): δ 152.9, 151.9, 151.3, 141.2, 136.9, 123.1, 122.4, 121.0, 120.0, 115.7, 70.3, 35.3, 35.1, 31.6, 31.6. HR-ESI-MS m/z = 476.3624 [M+H]⁺ (calc. for C₃₁H₄₆N₃O₄ 476.3635).

Figure S103 ¹H NMR (CDCl₃, 400 MHz) of S12
Figure S104 $^{13}$C NMR (CDCl$_3$, 101 MHz) of S12

Figure S105 COSY NMR (CDCl$_3$) of S12
Figure S106 HSQC NMR (CDCl₃) of S12

Figure S107 HMBC NMR (CDCl₃) of S12
Rotaxane 6 (30.0 mg, 0.03 mmol) was dissolved in CH$_2$Cl$_2$ (1.0 mL). CF$_3$CO$_2$H (0.5 mL) was added and the mixture was stirred for 16 h at rt. The reaction mixture was diluted with CH$_2$Cl$_2$ (10 mL), washed with saturated NaHCO$_3$(aq) (5 mL), brine (5 mL), dried (MgSO$_4$), filtered and the solvent removed \textit{in vacuo}. Chromatography (petrol and 0 to 10% Et$_2$O) gave S13 as a white foam (11.0 mg, 82%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.79 (d, $J$ = 15.5, 1H, H$_d$), 7.51 (br. s, 2H, H$_g$), 7.46 (t, $J$ = 1.7, 1H, H$_b$) 7.39 (d, $J$ = 1.7, 2H, H$_c$), 7.34 (br. s, 1H, H$_h$), 7.21 (br. s, 1H, H$_i$), 6.57 (d, $J$ = 15.5, 1H, H$_e$), 1.35 (s, 18H, H$_a$), 1.34 (s, 18H, H$_i$). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 164.1, 151.7, 151.4, 143.3, 137.5, 134.0, 124.4, 122.3, 120.3, 118.6, 114.5, 35.0, 34.9, 31.4, 31.4. HR-ESI-MS $m/z$ = 448.3570 [M+H]$^+$ (calc. for C$_{31}$H$_{46}$NO 448.3574).

Figure S108 $^1$H NMR (CDCl$_3$, 500 MHz) of S13
Figure S109 JMOD NMR (CDCl₃, 126 MHz) of S13

Figure S110 COSY NMR (CDCl₃) of S13
Figure S111 HSQC NMR (CDCl₃) of S13

Figure S112 HMBC NMR (CDCl₃) of S13
5. Single crystal X-ray analysis of rotaxanes 4, 5, 6 and 8

Crystals of 4 were grown by vapour diffusion of Et₂O into a CH₂Cl₂ solution. Crystals of 5, 6 and 8 were grown by vapour diffusion of pentane into an Et₂O solution.

Data were collected at 100 K using a FRES+ HF diffractometer equipped with a Saturn 724+ enhanced sensitivity detector. Cell determination, data collection, data reduction, cell refinement and absorption correction were performed with CrysalisPro. The structures 4 and 8 were solved using SUPERFLIP,[8,9] 5 was solved using ShelXT,[10] and 6 was solved using ShelXS.[11] All structures were refined against F₂ using anisotropic thermal displacement parameters for all non-hydrogen atoms using ShelXL[10] and software packages within. Hydrogen atoms were placed in calculated positions, except structure 5 H(1) which was located in the difference map, and all were refined using a riding model.
**Figure S113** Ellipsoid plot of the asymmetric unit of 4 (ellipsoids shown at 50% probability). Hydrogen atoms omitted for clarity.

| Property                        | Value                                      |
|---------------------------------|--------------------------------------------|
| Compound                        | 4                                          |
| CCDC                            | 1890755                                    |
| Empirical formula               | C_{63}H_{79}N_{5}O_{3}                     |
| Formula weight                  | 954.31                                     |
| Temperature/K                   | 293(2)                                     |
| Crystal system                  | monoclinic                                 |
| Space group                     | P2_1/n                                     |
| a/Å                             | 13.8964(7)                                 |
| b/Å                             | 21.8200(10)                                |
| c/Å                             | 18.2565(9)                                 |
| α/°                             | 90                                         |
| β/°                             | 94.479(5)                                  |
| γ/°                             | 90                                         |
| Volume/Å³                       | 5518.8(5)                                  |
| Z                               | 4                                          |
| ρ_{calcd}/g/cm³                 | 1.149                                      |
| μ/mm⁻¹                          | 0.070                                      |
| F(000)                          | 2064.0                                     |
| Crystal size/mm³                | 0.055 × 0.05 × 0.015                       |
| Radiation                       | MoKα (λ = 0.71075)                         |
| 2θ range for data collection/°  | 4.752 to 52.744                            |
| Index ranges                    | -17 ≤ h ≤ 17, -27 ≤ k ≤ 27, -22 ≤ l ≤ 22  |
| Reflections collected           | 63066                                      |
| Independent reflections         | 11291 [R_{int} = 0.0677, R_{sigma} = 0.0463] |
| Data/restraints/parameters      | 11291/0/656                                |
| Goodness-of-fit on F²            | 1.004                                      |
| Final R indexes [I>=2σ(I)]      | R₁ = 0.0543, wR₂ = 0.1189                 |
| Final R indexes [all data]      | R₁ = 0.0731, wR₂ = 0.1284                 |
| Largest diff. peak/hole / e Å⁻³ | 0.54/-0.25                                |
**Figure S114** Ellipsoid plot of the asymmetric unit of 5 (ellipsoids shown at 50% probability). Hydrogen atoms omitted for clarity.

| Property                                      | Value                        |
|-----------------------------------------------|------------------------------|
| Compound                                      | 5                            |
| CCDC                                          | 1890756                      |
| Empirical formula                             | C_{63}H_{79}N_{3}O_{3}       |
| Formula weight                                | 926.29                       |
| Temperature/K                                 | 100(2)                       |
| Crystal system                                | orthorhombic                 |
| Space group                                   | Pca2_1                       |
| a/Å                                           | 17.0247(4)                   |
| b/Å                                           | 26.2343(10)                  |
| c/Å                                           | 12.4688(4)                   |
| α/°                                           | 90                           |
| β/°                                           | 90                           |
| γ/°                                           | 90                           |
| Volume/Å³                                     | 5569.0(3)                    |
| Z                                             | 4                            |
| ρ_{calc}/g/cm³                                | 1.105                        |
| μ/mm⁻¹                                        | 0.067                        |
| F(000)                                        | 2008.0                       |
| Crystal size/mm³                              | 0.2 × 0.07 × 0.035           |
| Radiation                                     | MoKα (λ = 0.71075)           |
| 2θ range for data collection/°                | 3.92 to 52.746               |
| Index ranges                                  | -11 ≤ h ≤ 21, -18 ≤ k ≤ 32, -15 ≤ l ≤ 15 |
| Reflections collected                         | 21233                        |
| Independent reflections                       | 11078 [R_{int} = 0.0474, R_\sigma = 0.0902] |
| Data/restraints/parameters                    | 11078/1/637                  |
| Goodness-of-fit on F²                          | 1.026                        |
| Final R indexes [I>2σ (I)]                   | R_1 = 0.0738, wR_2 = 0.1496  |
| Final R indexes [all data]                    | R_1 = 0.1213, wR_2 = 0.1810  |
| Largest diff. peak/hole / e Å⁻³               | 0.31/-0.24                  |
**Figure S115** Ellipsoid plot of the asymmetric unit of 6 (ellipsoids shown at 50% probability). Hydrogen atoms omitted for clarity.

A "B–level" alert was detected using the IUCR checkcif algorithm. This was determined to be due to the geometry of the acrylamide combined with the macrocycle orientation which forces the amide proton and one of the alkene protons into close proximity. Thus, this alert is not a crystallographic error but an unusual feature of the interlocked structure which sterically constrains the covalent subcomponents in an otherwise energetically disfavoured arrangement.

| Compound | 6 |
|----------|---|
| CCDC     | 1890757 |
| Empirical formula | C₆₁H₇₅N₃O₅ |
| Formula weight | 930.24 |
| Temperature/K | 100(2) |
| Crystal system | monoclinic |
| Space group | P2₁ |
| a/Å | 10.8046(5) |
| b/Å | 16.8432(5) |
| c/Å | 15.2219(6) |
| α/° | 90 |
| β/° | 105.545(4) |
| γ/° | 90 |
| Volume/Å³ | 2668.80(19) |
| Z | 2 |
| ρ calc/g/cm³ | 1.158 |
| μ/mm⁻¹ | 0.073 |
| F(000) | 1004.0 |
| Crystal size/mm³ | 0.1 × 0.05 × 0.02 |
| Radiation | MoKα (λ = 0.71075) |
| 2θ range for data collection/° | 5.876 to 52.744 |
| Index ranges | -13 ≤ h ≤ 13, -20 ≤ k ≤ 21, -19 ≤ l ≤ 19 |
| Reflections collected | 25741 |
| Independent reflections | 10822 [R_int = 0.0558, Rsigma = 0.0948] |
| Data/restraints/parameters | 10822/1/634 |
| Goodness-of-fit on F² | 1.042 |
| Final R indexes [I>=2σ (I)] | R₁ = 0.0718, wR₂ = 0.1599 |
| Final R indexes [all data] | R₁ = 0.1045, wR₂ = 0.1737 |
| Largest diff. peak/hole / e Å⁻³ | 0.47/-0.21 |
Figure S116 Ellipsoid plot of the asymmetric unit of 8 (ellipsoids shown at 50% probability). Hydrogen atoms omitted for clarity, except for H11C, H11D, H15L and H15M.

| Compound       | 8 |
|----------------|---|
| CCDC           | 1890758 |
| Empirical formula | C_{64}H_{83}N_{3}O_{4} |
| Formula weight | 958.33 |
| Temperature/K  | 100(2) |
| Crystal system | triclinic |
| Space group    | P-1 |
| a/Å            | 15.5175(6) |
| b/Å            | 16.9490(5) |
| c/Å            | 23.3325(6) |
| α/°            | 105.257(2) |
| β/°            | 100.079(3) |
| γ/°            | 93.338(3) |
| Volume/Å^3     | 5793.7(3) |
| Z              | 4 |
| ρ_{calc}/g/cm^3 | 1.099 |
| μ/mm⁻¹         | 0.067 |
| F(000)         | 2080.0 |
| Crystal size/mm³ | 0.1 × 0.05 × 0.01 |
| Radiation      | MoKα (λ = 0.71075) |
| 2θ range for data collection/° | 5.804 to 52.744 |
| Index ranges   | -19 ≤ h ≤ 17, -20 ≤ k ≤ 21, -29 ≤ l ≤ 25 |
| Reflections collected | 51024 |
| Independent reflections | 22793 [R_{int} = 0.0432, R_{sigma} = 0.0799] |
| Data/restraints/parameters | 22793/0/1309 |
| Goodness-of-fit on F^2 | 1.155 |
| Final R indexes [I>=2σ (I)] | R_1 = 0.0877, wR_2 = 0.1845 |
| Final R indexes [all data] | R_1 = 0.1236, wR_2 = 0.1990 |
| Largest diff. peak/hole / e Å⁻³ | 0.89/-0.50 |
6. Optimisation of reaction conditions for the rearrangement reaction

Table S1 Optimisation of the formation of 5 with respect to solvent, temp. and additive.

| Entry | Time  | Solvent          | Temp | Additive      | Conversion | Ratio 4 : 5 |
|-------|-------|------------------|------|---------------|------------|-------------|
| 1     | 16 h  | CH₂Cl₂           | RT   | NPr₂Et (2 eq.) | 100%       | 90 : 10     |
| 2     | 16 h  | CH₂Cl₂ + 10% H₂O| RT   | NPr₂Et (2 eq.) | 100%       | 90 : 10     |
| 3     | 16 h  | CH₂Cl₂ + 10% H₂O| RT   | -             | trace - 100%* | 60 : 40     |
| 4     | 24 h  | CH₂Cl₂           | RT   | -             | 0          | -           |
| 5     | 24 h  | THF              | RT   | -             | 0          | -           |
| 6     | 48 h  | THF + 10% H₂O    | RT   | -             | 24 - 100%* | <1 : >99    |
| 7     | 48 h  | THF + 10% H₂O    | RT   | KF (0.9 eq.)  | 100%       | <1 : >99    |
| 8     | 48 h  | THF + 10% H₂O    | RT   | TBAF (0.9 eq.)| 100%±       | 50 : 50     |
| 9b    | 20 min| THF + 10% H₂O    | 80 °C| -             | 66 - 80%*  | <1 : >99    |
| 10b   | 20 min| THF + 10% H₂O    | 80 °C| KF (0.9 eq)   | >99%       | 4.96        |
| 11b   | 20 min| THF + 10% H₂O    | 80 °C| TBAF (0.9 eq) | 100%       | 57:43       |
| 12b   | 1 h   | THF + 10% H₂O    | 70 °C| KF (0.9 eq)   | 100%       | <1 : >99    |
| 13c   | 1 h   | THF + 10% H₂O    | 70 °C| KF (0.9 eq)   | 100%       | <1 : >99    |
| 14b   | 1 h   | THF + 10% H₂O    | 70 °C| KNO₃ (0.9 eq) | 100%       | 7:93        |
| 15b   | 1 h   | THF + 10% H₂O    | 70 °C| TBAF (0.9 eq) | 100%       | 8 : 92      |
| 16bd  | 1 h   | THF + 10% H₂O    | 70 °C| KF (0.9 eq)   | 100%       | 72 : 28     |
| 17bd  | 1 h   | THF + 10% H₂O    | 70 °C| KNO₃ (0.9 eq) | 100%       | >99 : <1     |

*Determined by 1H NMR. *Performed in a microwave reactor. *Performed under thermal conditions in an oil bath. *[Cu(MeCN)₄]PF₆ was replaced by CuSO₄/NaAsc. *Conversion varied run-to-run. *Decomposition to an unknown product was also observed.

The role of KF remains unclear; neither TBAF (entries 8, 11 and 15) nor KNO₃ (entries 14 and 17) produce the same outcome as KF under the same conditions, suggesting that both the cation and anion play a role. Interestingly at 70 °C, TBAF and KF appear more comparable (entry 12 vs 15). (note: at 80 °C [Entry 11] the lower selectivity of TBAF may be due to fluoride-mediated decomposition of the tetrabutyl ammonium cation) [12] Interestingly, when [Cu(MeCN)₄]PF₆ is replaced by CuSO₄/Na-ascorbate, KNO₃ outperforms KF, suggesting that the role of the inorganic salt is quite complex.
7. **Kinetic Study of the reaction of 1a, 2a and 3a.**

1a (7.3 mg, 0.0153 mmol), [Cu(MeCN)₄]PF₆ (5.5 mg, 0.0147 mmol), 2a (4.3 mg, 0.0184 mmol), and 3a (4.5 mg, 0.0184 mmol) were dissolved in D₂O-THF-d₈ (1:9, 1.2 mL). The solution was passed through a Celite plug and 0.6 ml was transferred into a NMR tube and analysed by ¹H NMR at 2 h intervals. The disappearance of the peak at 7.16 ppm (d, J = 1.7, 2H) and the appearance of the peak at 7.91 (d, J = 1.7 Hz, 1H) was monitored.

**Figure S117** Stacked partial ¹H NMRs (400 MHz, THF-d₈/D₂O 9:1) showing formation of 5 and consumption of 2a.

**Figure S118** Consumption of 2a and formation of 5 based on their normalised integrals with respect to the residual protonated THF signal (3.62 ppm)
8. Control experiment: axle formation under conditions optimised for the formation of acrylamide rotaxane 5

KF$_{\text{aq}}$ (0.2 mL, 0.1 M), was added to a solution of 3a (7.3 mg, 0.030 mmol), 2a (6.9 mg, 0.030 mmol) 1c (14.3 mg, 0.025 mmol) and $[\text{Cu(MeCN)}_4]\text{PF}_6$ (8.9 mg, 0.024 mmol) in THF (1.8 mL) in a microwave vial. The orange mixture was stirred at 70 °C (µW) for 1 h. The reaction mixture was diluted with CH$_2$Cl$_2$ (10 mL) and washed with EDTA-NH$_3$ solution (10 mL). The aqueous layer extracted with CH$_2$Cl$_2$ (2 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried (MgSO$_4$), filtered and the solvent removed in vacuo. Analysis by $^1$H NMR revealed S12 to be the sole product.

$\text{OH}$
$\text{N}_3$
$\text{[Cu(MeCN)}_4]\text{PF}_6$
$\text{THF/KF}_{\text{aq}}$ 9/1

$\text{1c}$

$\text{3a}$
$\text{2a}$
$\text{1c}$
$\text{S12}$

$\text{OH}$
$\text{N}_3$
$\text{N}_3$
$\text{N}_3$

$\text{1c}$

$\text{3a}$
$\text{2a}$
$\text{1c}$
$\text{S12}$

Figure S119 Stacked partial $^1$H NMR (400 MHz, CDCl$_3$) spectra of (from top to bottom) 1c, the crude reaction mixture, triazole axle S12 and acrylamide S13.
KF\textsubscript{(aq)} (0.2 mL, 0.1M), was added to a solution of 3a (7.3 mg, 0.030 mmol), 2a (6.9 mg, 0.030 mmol) and [Cu(MeCN)]\textsubscript{4}PF\textsubscript{6} (8.9 mg, 0.024 mmol) in THF (1.8 mL) in a microwave vial. The yellow mixture was stirred at 70 °C (µW) for 1 h. The crude reaction mixture was diluted with CH\textsubscript{2}Cl\textsubscript{2} (10 mL) and washed with EDTA-NH\textsubscript{3} solution (10 mL). The aqueous layer was extracted with CH\textsubscript{2}Cl\textsubscript{2} (2 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried (MgSO\textsubscript{4}), filtered and the solvent removed \textit{in vacuo}. Analysis by \textsuperscript{1}H NMR revealed S12 to be the sole product.

\textbf{Figure S120} Stacked partial \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) of (from top to bottom) the crude reaction mixture, triazole axle S12 and acrylamide S13.
9. Mechanistic studies: rearrangement of triazolide 12 under aqueous conditions

To investigate whether triazolide 12 is an intermediate *en route* to acrylamide rotaxane 11 we explored the reaction of 12 under various conditions and analysed the results by $^1$H NMR:

**Step 1:** $\text{Pr}_2\text{NEt (40.0 µl, 0.23 mmol)}$ was added to a solution of 3c (25.6 mg, 0.10 mmol), 2a (23.1 mg, 0.10 mmol), 1a (48.0 mg, 0.10 mmol) and $\text{[Cu(MeCN)]}_4\text{PF}_6$ (36.6 mg, 0.098 mmol) in CH$_2$Cl$_2$ (8.0 mL). The deep-red solution was washed with H$_2$O (10 mL), brine (10 mL), dried (MgSO$_4$) and the solvent removed *in vacuo*. $^1$H NMR analysis of the residue confirmed that the starting materials had been consumed to produce a new species whose $^1$H NMR resonances are consistent with triazolide 12; four signals are observed for macrocycle protons H$_C$ and H$_H$ ($\sim$ 6.2 ppm) due to the presence of the axle stereogenic centre, no triazole resonance was observed, and the spectrum is distinct from that of the $\text{[Cu(11)]}^+$. MS analysis of a portion of the solution supports this assignment ($m/z =1030.9$ [M+H]$^+$; calc. for C$_{64}$H$_{80}$CuN$_3$O$_3$ = 1030.9).

**Step 2A:** The residue from **step 1** was dissolved in a mixture of KF$_{6(aq)}$ (0.1 M, 0.1 mL) and THF (0.9 mL). The orange mixture was stirred at 70 °C ($µW$) for 1 h. The reaction mixture was diluted with CH$_2$Cl$_2$ (20 mL) and washed with EDTA-NH$_3$ solution (10 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO$_4$) and the residue analysed by $^1$H NMR.

**Step 2B:** The residue from **step 1** was dissolved in a mixture of KF$_{6(aq)}$ (0.2 M, 0.05 mL), HPF$_{6(aq)}$ (0.2 M, 0.05 mL) and THF (0.9 mL). The orange mixture was stirred at 70 °C ($µW$) for 1 h. The reaction mixture was diluted with CH$_2$Cl$_2$ (20 mL) and washed with EDTA-NH$_3$ solution (10 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO$_4$) and the residue analysed by $^1$H NMR.

**Step 2C:** The residue from **step 1** was dissolved in a mixture of HPF$_{6(aq)}$ (0.13 M, 0.1 mL, 1 eq.) and THF (0.9 mL). The orange mixture was stirred at 70 °C ($µW$) for 1 h. The reaction mixture was diluted with CH$_2$Cl$_2$ (20 mL) and washed with EDTA-NH$_3$ solution (10 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO$_4$) and the residue analysed by $^1$H NMR.

**Step 2D:** The residue from **step 1** was dissolved in a mixture of HPF$_{6(aq)}$ (0.13 M, 0.1 mL, 1 eq.) and THF (0.9 mL). The orange mixture was stirred for 1 h at rt. The reaction mixture was diluted with CH$_2$Cl$_2$ (20 mL) and washed with EDTA-NH$_3$ solution (10 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO$_4$) and the solvent removed *in vacuo*. The residue was analysed by $^1$H NMR.
Production of 11 was confirmed by $^1$H NMR. In all cases, triazole rotaxane S9 was not observed. Due to broadening of the signals corresponding to triazolide 12, conversion could not be quantified in the case of step 2A. However, the presence of the doublet at 6.21 ppm which is assigned to 12, indicates that consumption of 12 is incomplete.

**Control experiments**

To rule out the conversion of 12 to rotaxane S9 followed by reaction to produce 11, control experiments with rotaxane S9 were performed under the same conditions:

**Conditions A:** Triazole rotaxane S9 (1.6 mg, 0.0017 mmol) in THF (200 µL) was treated with a solution of HPF$_6$(aq) (20 µL, 0.08 M, 0.0017 mmol) in a sealed microwave vial. The mixture was stirred at 70 °C (µW) for 1 h. The reaction was diluted with CH$_2$Cl$_2$ (10 mL) and washed with EDTA-NH$_3$(aq) (5 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO$_4$), filtered and the solvent removed *in vacuo*. Analysis of the residue by $^1$H NMR showed some decomposition but no formation of 11.

**Conditions B:** Triazole rotaxane S9 (1.6 mg, 0.0017 mmol) and [Cu(MeCN)$_4$]PF$_6$ (0.6 mg, 0.0016 mmol) were dissolved in THF (200 µL) and treated with a solution of HPF$_6$(aq) (20
μL, 0.08 M, 0.0017 mmol), in a sealed microwave vial. The mixture was stirred at 70 °C (μW) for 1 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with EDTA-NH₃(aq) (5 mL). The aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried (MgSO₄), filtered and the solvent removed in vacuo. Analysis of the residue by ¹H NMR showed a small amount of decomposition but no formation of 11.

Figure S122 Stacked partial ¹H NMR (400 MHz, CDCl₃) of the product of conditions A and B, compared with triazole rotaxane S9.
10. Mechanistic studies: rearrangements triggered by Tf₂O under anhydrous conditions

i. In situ ¹H NMR analysis of the reaction of the product of 1a, 2a and 3c with Tf₂O

To demonstrate the key role of the OH of triazolide 12 as a leaving group and to attempt to observe the proposed cumulene intermediate we explored the reaction of 12 with Tf₂O under anhydrous conditions and analysed the results by ¹H NMR:

**Step 1:** Pr₂NEt (70 µl, 0.40 mmol) was added to a solution of 3c (25.8 mg, 0.10 mmol), 2a (23.1 mg, 0.10 mmol), 1a (47.8 mg, 0.10 mmol) and [Cu(MeCN)₂]PF₆ (36.8 mg, 0.099 mmol) in CDCl₃ (4.0 mL) in a sealed microwave vial, and the mixture stirred at rt for 45 min. ¹H NMR analysis of the reaction mixture confirmed that the starting materials had been consumed to produce a new species whose ¹H NMR resonances are consistent with triazolide 12; four signals are observed for macrocycle protons H₆ and H₈ (~ 6.2 ppm) due to the presence of the axle stereogenic centre, no triazole resonance was observed, and the spectrum is distinct from that of the [Cu(11)]⁺. MS analysis of a portion of the solution supports this assignment (m/z =1030.9 [M+H]+; calc. for C₆₆H₇₀CuN₅O₃ = 1030.9).

**Step 2:** A portion (2.0 mL) was removed and treated with Tf₂O (0.1 M in CDCl₃, 0.05 mL, 0.05 mmol) and the reaction mixture was stirred at rt for 20 mins. ¹H NMR analysis of the reaction mixture reveals the species assigned as 12 has largely been consumed to produce a new major species whose ¹H NMR resonances are consistent with cumulene 13; macrocycle protons H₆ and H₈ (8.3 ppm and 8.1 ppm respectively) appear as single environments suggesting the axle stereogenic unit has been lost. This assignment is supported by LCMS analysis of a portion of the reaction mixture; the major species observed has m/z =984.8 (retention time = 3.02 min) which is consistent with 13 (calc. for C₆₆H₇₀CuN₅O₃ = 984.6). Fractions were also observed corresponding to macrocycle 1a (2.14 min), rearranged product 11 and also 12-OH, suggesting that S14 persists in the reaction mixture ([M-OTf]⁻), or that the corresponding cation is a stable intermediate in the case of 12.

**Step 3a:** A portion of the solution produced in **Step 2** (0.5 mL, 0.0125 mmol) was treated with KCN (7.2 mg, 0.110 mmol) in H₂O (1 mL) and the mixture stirred at rt for 16 h. The reaction mixture was diluted with CH₂Cl₂ (20 mL), washed with H₂O (3 × 3 mL), dried (MgSO₄) and the solvent removed under vacuum. The crude residue was analysed by ¹H NMR to reveal 11 as the major product (11 : S12 ~ 95 : 5).

**Step 3b:** A portion of the solution produced in **Step 2** (0.5 mL, 0.0125 mmol) was treated with H₂O (1 mL) and the mixture stirred at rt for 16 h. The reaction mixture was diluted with CH₂Cl₂ (20 mL), washed with H₂O (3 × 3 mL), dried (MgSO₄) and the solvent removed under vacuum. The crude residue was analysed by ¹H NMR to reveal a spectrum remarkably
similar to that at the end of step 2, albeit sharper resonances were observed. This suggests that 13 survives treatment with H$_2$O in the absence of KCN.

**Control experiment:** A portion of the solution produced in **step 1** (0.5 mL, 0.0125 mmol) was treated with TfOH (1.1 μL, 0.0125 mmol), and diluted with CDCl$_3$ (25 μL). No significant change was observed by $^1$H NMR (**control i**). The solution was treated with KCN (7.1 mg, 0.110 mmol) in H$_2$O (1 mL) and stirred for 16 h. The reaction mixture was diluted with CH$_2$Cl$_2$ (20 mL), washed with H$_2$O (3 × 3 mL), dried (MgSO$_4$) and the solvent removed *in vacuo*. $^1$H NMR analysis (**control ii**) revealed the major product to be triazolide 12 (11 and S12 observed in trace amounts).

---

**Figure S123** Stacked partial $^1$H NMR (400 MHz, CDCl$_3$) of the products of **step 1**, **step 2**, **step 3a**, **step 3b**, **control i**, and **control ii**, compared with purified 11 and S12. At the end of **step 3a**, the ratio of 11 : S12 = 95:5.

**Figure S124** LCMS trace (UV = 254 nm, C18 column [1 : 4 MeCN-H$_2$O + 0.2% HCO$_2$H → MeCN + 0.2% HCO$_2$H]), of the reaction mixture at the end of step 2. Note Peak D did not appear in the total ion count.

S90
These experiments suggest that Tf$_2$O triggers the extrusion of N$_2$ from triazolide 12 and provide evidence that a cumulene of the form 13 is an intermediate in the reaction. The control experiment with TfOH rules out the in situ hydrolysis of Tf$_2$O to produce acid that then triggers the rearrangement. The slow reaction of 13 with H$_2$O in contrast with KCN$_{(aq)}$ suggests that the Cu$^+$ ion stabilises the cumulene structure, although the lower pH of the KCN solution may also play a role in accelerating the nucleophilic attack. These results also suggest that the hydrolysis of the cumulene intermediate under the optimised reaction conditions is accelerated by H$^+$, given that 12 rearranges to 11 rapidly at rt in the presence of HPF$_6$ without added KF.
ii. *In situ* $^1$H NMR analysis of the reaction of 1a, 2a and 3a followed by Tf$_2$O

To provide evidence that the same mechanism observed for 12 is in operation with other substrates we investigated the reaction of 1a, 2a and 3a under anhydrous conditions with Tf$_2$O and analysed the results by $^1$H NMR:

Following the same procedure as above with 1a, 2a and 3a gave a similar outcome as above. After step 1 a new species was observed that was consistent with triazolide S15. Treatment with Tf$_2$O (step 2) led to $\sim$70% conversion of S15 to produce a species assigned as cumulene S17 (ratio of signals at $\sim$5.0 ppm [2H of S15] to doublet at $\sim$8.2 ppm [2H of S16] = 1 : 2.6). Treatment of this product with KCN$_{aq}$ (step 3a) gave acrylamide 5 as the major product (5 : 4 = 90 : 10). Conversely, treatment of a solution of cumulene S17 with H$_2$O (step 3b) resulted in incomplete consumption of S17 to produce 5 (5 : 4 = 90 : 10).

---

**Figure S125** Stacked partial $^1$H NMR (400 MHz, CDCl$_3$) of step 1, step 2, step 3a (5 : 4 90:10) and step 3b (incomplete, 5 : 4 90:10), compared with spectra of isolated 5 and 4.
11. Preliminary computational analysis of the mechanism of the rearrangement process

In order to provide further information on the pathway of the rearrangement process and in an attempt to identify the role of the CuI ion in the process, we carried out a preliminary computational investigation of the reaction pathway.

i. Preparation of a truncated model \textbf{Ia} of triazolide S15

Preliminary molecular modelling was carried out to assess the feasibility of the mechanism proposed based on the studies in sections S6-S10. Due to the large size of the interlocked intermediates of the reaction a truncated model was used.

A model of triazolide S15 was prepared using Spartan '10 (Wavefunction Ltd.) and a conformation search performed using mechanics (MMFF, vacuum). The lowest energy structure identified was optimised using the PM6 semi-empirical method (vacuum). The model was then truncated to provide a starting point (\textbf{Ia}) for DFT calculations below (Figure S126).

![Figure S126](image)

\textbf{Figure S126} a) Structures and b) models of S15 and truncated triazolide model \textbf{Ia}

ii. DFT evaluation of the pathway of N\textsubscript{2} loss from truncated triazolide model \textbf{Ia}

Gaussian '09 (DFT-rB3LYP-631G) was used for subsequent calculations with the default H\textsubscript{2}O solvation model.\textsuperscript{[13]} The reaction pathway obtained, computed structures obtained and their relative energies are shown in Figure S127 and Figure S128.

![Figure S127](image)

\textbf{Figure S127} Intermediates in the calculated path from truncated axle \textbf{Ia} to cumulene VI.
Figure S128 Calculated (Gaussian '09, rB3LYP-631G, default H₂O solvent model) structures and energies of intermediates IIa to VIIa.
H\textsuperscript{+} was added to either N\textsuperscript{3} of the triazole or the OH of structure Ia and the geometry of these species was optimised. No stable structure could be identified for the O-protonated species in which the C-O bond was maintained. The energy difference between N-protonated (IIa) and O-protonated (IIIa) models was found to be 17.9 kJmol\textsuperscript{-1}. The departed H\textsubscript{2}O leaving group was removed from the model of the carbocation and the geometry was optimised again (IVa). This structure was used as a starting point for further calculations and its computed energy was used as the new baseline.

A scan (unrestricted, 10 steps of 0.1 Å) was performed using the C-N\textsuperscript{3} bond length as the redundant coordinate. The outcome of this scan indicated that an energy maximum was reached with C-N\textsuperscript{3} = 1.82276 Å (Figure S129a). A transition state calculation was performed using the maximum energy structure found in this scan as a starting point. A species (TS-Va) with a single imaginary frequency was identified. An IRC calculation (20 steps forward and 20 steps reverse, final structures optimised, Figure S129b) confirmed that this transition state connected the starting cation (IV) and a cumulene species (VI) in which N\textsubscript{2} had been extruded. The reaction is exergonic by 44.9 kJmol\textsuperscript{-1} and TS-Va lies 77.7 kJmol\textsuperscript{-1} above cation Va.

![Figure S129](image)

**Figure S129** a) Plot of the scan (unrestricted with N\textsubscript{1}-N\textsubscript{2} as redundant coordinate) of the N\textsubscript{1}-N\textsubscript{2} length in 0.1 Å steps vs energy. b) Plot of the IRC scan for TS-V.

Examining the calculated structure of cumulene (VI), it is worth noting that a) the Cu\textsuperscript{+}-ion remains associated with the \( \pi \)-system and b) the C-C-C-N unit is not linear. This may indicate that the true structure lies somewhere between the limiting resonance structures in which the Cu\textsuperscript{+}-ion engages the cumulene through a \( \pi \)-metal interaction and a \( \sigma \)-metal interaction (Figure S127Figure S129).

We were unable to locate a transition state for the stepwise opening of the triazole to give vinyl diazonium VIIa, the expected intermediate if N\textsubscript{2} loss were to proceed in a stepwise manner. This is unsurprising as this species was found to lie 139.8 kJmol\textsuperscript{-1} above that of cation IVa (i.e. 62.1 kJmol\textsuperscript{-1} above TS-Va) when prepared and optimised directly. The IRC plot shows an inflection before TS-Va and examining the computed structures, it is clear that whereas early in the process the reaction coordinate is primarily associated with the stretching of the N\textsubscript{1}-N\textsubscript{2} bond, as would be expected en route to VIIa, the inflection point is associated with the stretching of the C-N\textsuperscript{3} bond starting to contribute to the pathway.
iii. DFT evaluation of the pathway of $N_2$ loss from truncated triazole model Ib

Finally, for comparison, we repeated the above calculations for the corresponding reaction of triazole starting material Ib (pathway shown in Figure S130, calculated structures and energies shown in Figure S131). The reaction of Ib was found to proceed via a stepwise pathway in which vinyl diazonium VIIb is an intermediate lying in a shallow minimum ~1 kJmol$^{-1}$ below the transition state which is itself found 49.1 kJmol$^{-1}$ above IVb. The transition state for loss of $N_2$ from VIIb was found to lie ~ 90.9 kJmol$^{-1}$ above this intermediate and thus, including the pre-equilibrium between IVb and VIIb, the transition state of the rate limiting loss of $N_2$ lies 139 kJmol$^{-1}$ above cation IVb. Furthermore, an IRC calculation suggests that the product of this pathway is best represented by limiting the limiting resonance structures shown rather than a cumulene structure analogous to VIa as migration of the C-H bond was not found to take place spontaneously during loss of $N_2$.

![Figure S130](image-url) Intermediates in the calculated path from truncated axle Ia to cumulene VI.

iv. Conclusions

Comparing the computed reaction pathways for loss of $N_2$ from Ia and Ib, the electron rich C-Cu$^1$ bond of the triazolide appears favour the opening of the triazole compared with the C-H bond of the simple triazole in three ways: i) the stability of the intermediate formed by protonation of the OH group (III) compared to the intermediate protonated on N (II) is enhanced by the Cu-C bond, biasing this pre-equilibration step towards key reactive intermediate III (IV); ii) the pathway of the ring opening process is altered as the electron rich Cu-C bond is eliminated during the loss of $N_2$, leading directly to a stable cumulene structure instead of a stepwise process via vinyl diazonium VIIa; iii) the C-H bond does not participate in $N_2$ loss. As a consequence, loss of $N_2$ leads to unstable vinyl cation product IX with a consequently higher reaction barrier.
Figure S131 Calculated (Gaussian '09, rB3LYP-631G, default H₂O solvent model) structures and energies of intermediates IIb to IXb.
12. References

[1] J. Hornung, D. Fankhauser, L. D. Shirtcliff, A. Praetorius, W. B. Schweizer, F. Diederich, *Chem. – A Eur. J.* **2011**, *17*, 12362.

[2] W. Zhu, D. Ma, *Chem. Commun.* **2004**, 888.

[3] J. J. Gassensmith, L. Barr, J. M. Baumes, A. Paek, A. Nguyen, B. D. Smith, *Org. Lett.* **2008**, *10*, 3343.

[4] E. A. Neal, S. M. Goldup, *Angew. Chem. Int. Ed.* **2016**, *55*, 12488.

[5] J. E. M. Lewis, R. J. Bordoli, M. Denis, C. J. Fletcher, M. Galli, E. A. Neal, E. M. Rochette, S. M. Goldup, *Chem. Sci.* **2016**, *7*, 3154.

[6] L. M. Urner, M. Sekita, N. Trapp, W. B. Schweizer, M. Wörle, J.-P. Gisselbrecht, C. Boudon, D. M. Guldi, F. Diederich, *European J. Org. Chem.* **2015**, *2015*, 91.

[7] Y. Itoh, R. Kitaguchi, M. Ishikawa, M. Naito, Y. Hashimoto, *Bioorg. Med. Chem.* **2011**, *19*, 6768.

[8] L. Palatinus, G. Chapuis, *J. Appl. Crystallogr.* **2007**, *40*, 786.

[9] L. Palatinus, S. J. Prathapa, S. Van Smaalen, *J. Appl. Crystallogr.* **2012**, *45*, 575.

[10] G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.* **2015**, *71*, 3.

[11] G. M. Sheldrick, *Acta Crystallogr. Sect. A Found. Crystallogr.* **2008**, *64*, 112.

[12] R. K. Sharma, J. L. Fry, *J. Org. Chem.* **1983**, *48*, 2112.

[13] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, *Gaussian 09* (Gaussian, Inc., Wallingford CT, 2009).