Appendix 2

The Synthesis of “Magic Ring” Rotaxanes using Olefin Metathesis

A2.1 Abstract

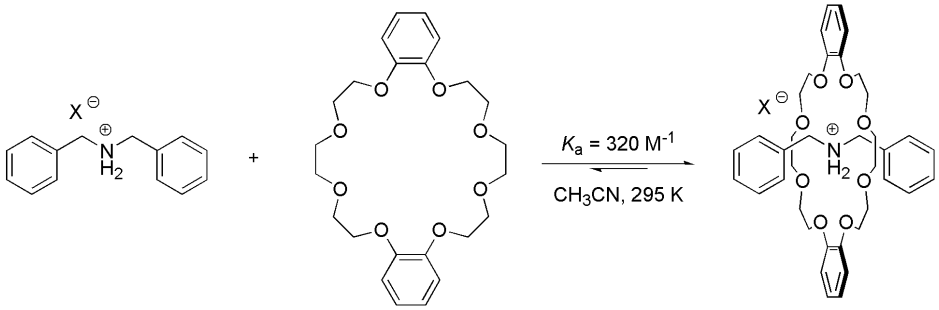
The Ru-catalyzed ring-closing metathesis (RCM) of crown ether-like diolefinic substrates around a dumbbell-shaped secondary ammonium ion affords [2]rotaxanes. The reversible nature of this process is demonstrated via “magic ring” synthesis, wherein, in the presence of a metathesis catalyst, the preformed olefin-containing macrocycle and dumbbell-shaped component equilibrate to form the hydrogen-bond stabilized [2]rotaxane in the presence of a metathesis catalyst.

A2.2 Introduction

Rotaxanes[1] are mechanically-interlocked molecules consisting of a dumbbell-shaped component around which one or more macrocycles are trapped. Although a majority of rotaxane syntheses to date have relied upon kinetic control, (*e.g.*, employing an irreversible final step) developments in dynamic covalent chemistry[2] have spurred an interest in thermodynamically-controlled rotaxane formation.[3,4] Reactions utilized for this purpose include imine and disulfide formation.[5] Olefin metathesis has been used in the thermodynamically-controlled synthesis of a [2]catenane,[6] and has also been applied to the anion-templated synthesis of a [2]rotaxane.[7]

One common supramolecular synthon in the preparation of interlocked molecules is the mutual recognition of secondary dialkylammonium ($R_2NH_2^+$) ions and suitably-sized crown ethers, most notably dibenzo[24]crown-8 (**A2.1**, Scheme A2.1).[8] We reasoned that this recognition motif can be coupled with the versatile reversible ring closing olefin metathesis reaction to promote rotaxane formation under thermodynamic control.

Scheme A2.1. Dialkylammonium ions show affinity toward binding crown ethers.

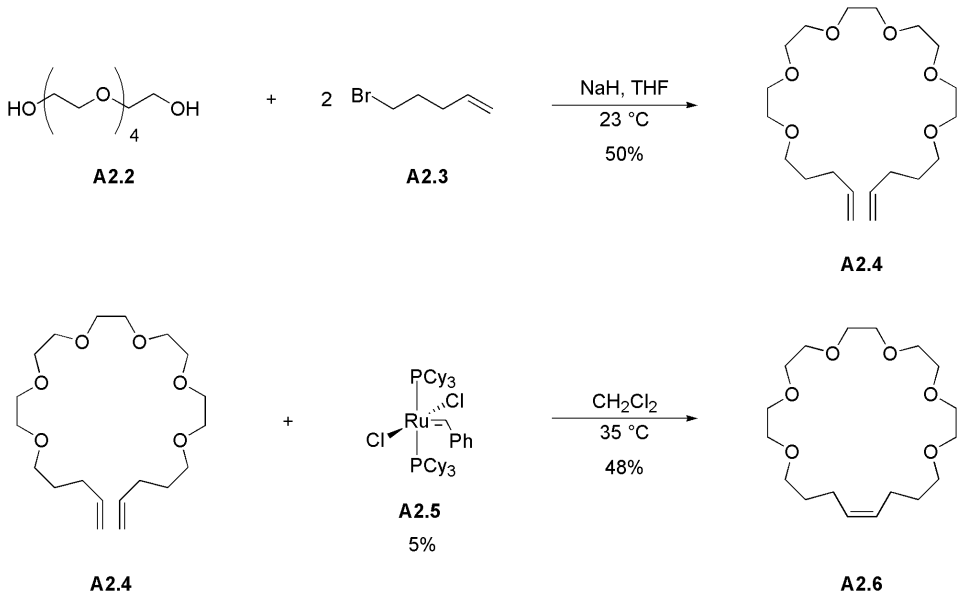


A2.1

A2.3 Rotaxane Synthesis and Characterization

To create a RCM substrate capable of mimicking the $R_2NH_2^+$ binding capability of dibenzo-crown ether **A2.1**, we designed an olefin-containing macrocycle that resembles a crown ether. Pentaethylene glycol (**A2.2**) was bis-alkylated with 5-bromo-1-pentene (**A2.3**) to afford terminal diolefin **A2.4** in moderate yield (Scheme A2.2). Treatment of **A2.4** with $(PCy_3)_2Cl_2Ru{=}CHPh$ (**A2.5**)[9] under dilute conditions (5 mM) gave the 24-membered olefinic crown ether analogue **A2.6** as a mixture of *E*- and *Z*-isomers.

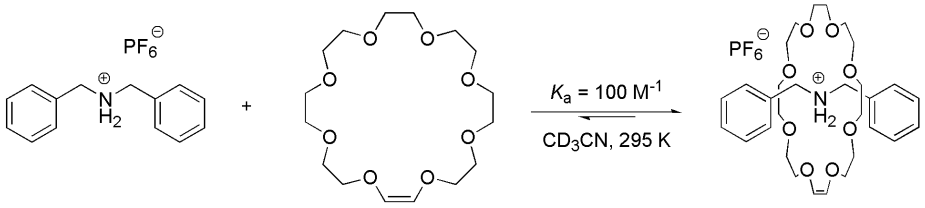
Scheme A2.2. The synthesis of macrocycle **A2.6**.



The ability of **A2.6** to bond ammonium ions was demonstrated by its interaction with dibenzylammonium hexafluorophosphate (Scheme A2.3). This resulted in the formation of a 1:1 complex with a threaded geometry, as revealed by ^{1}H NMR

spectroscopy. The association constant (K_a) for this process was determined via the single point method to be 100 M^{-1} (CD_3CN, 295 K), which compares favorably with the value of 320 M^{-1} reported for **A2.1** under similar conditions.[10,11] This reduced binding affinity is likely due to the loss of two ether O atoms on going from **A2.1** to **A2.6**, thereby decreasing the hydrogen bonding potential between the two components. Hydrogenation of **A2.6** affords saturated crown ether, which was shown to bind dibenzylammonium hexafluorophosphate with a K_a value of 90 M^{-1}. This value differs only slightly from that observed for **A2.6**, suggesting that the C–C double bond has little effect upon secondary ammonium ion binding.

Scheme A2.3. Interaction of macrocycle **A2.6** with an ammonium salt.

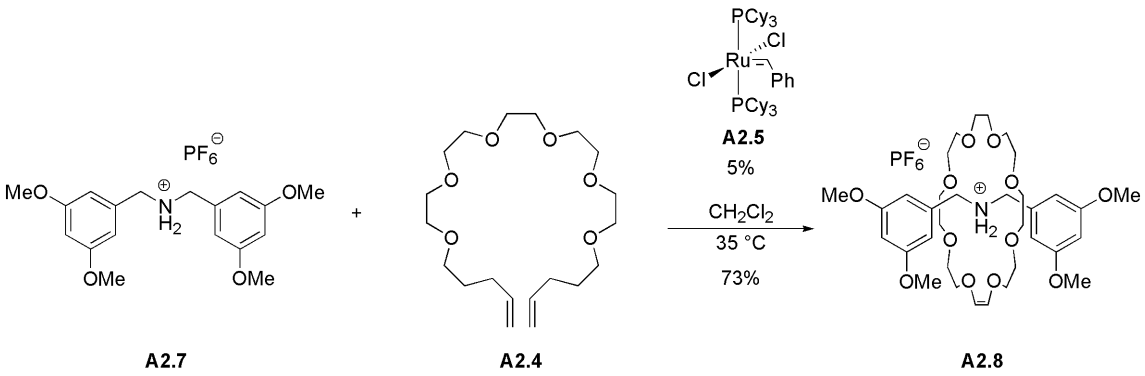


A2.6

Encouraged by these findings, we next attempted RCM of terminal diolefin **A2.4** in the presence of the end-capped ammonium ion, bis(3,5-dimethoxybenzyl)-ammonium hexafluorophosphate (**A2.7**, Scheme A2.4).[12] This reaction provided the corresponding [2]rotaxane **A2.8** as a mixture of *E* and *Z* olefin isomers in 73% yield. The significant templating effect of the $R_2NH_2^+$ ion is emphasized by comparison of the yield of the templated RCM reaction to its untemplated counterpart. Whereas the reaction in the absence of a template must be performed at 5 mM to avoid oligo/polymerization and affords only 48% yield of the desired macrocycle, it is possible to conduct the reaction in

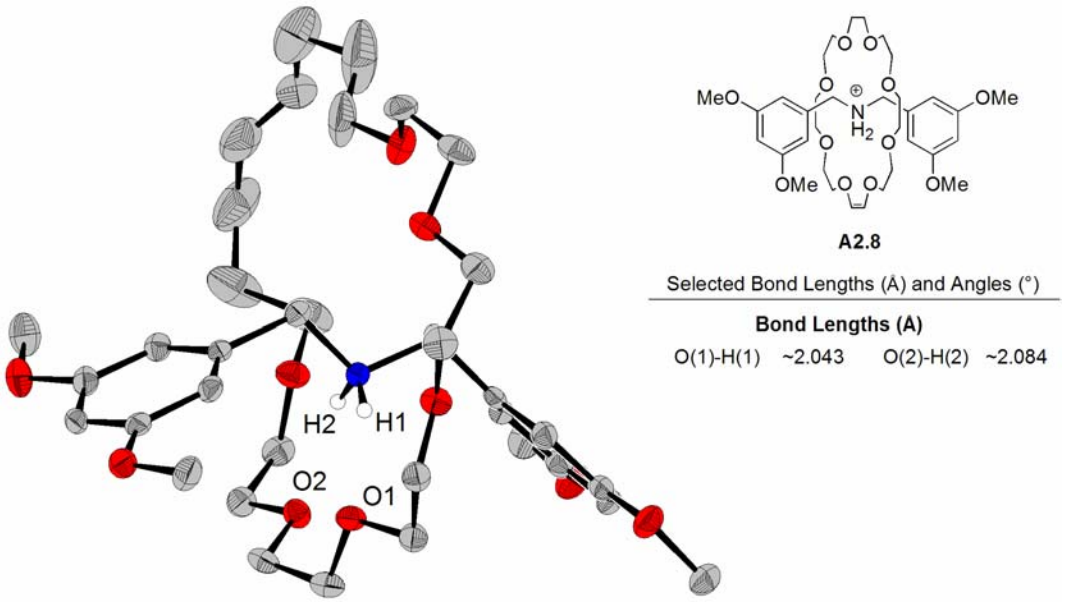
the presence of template at much higher concentration (ca. 100 mM in this case), and results in 73% yield of rotaxane.

Scheme A2.4. Synthesis of [2]rotaxane **A2.8**.



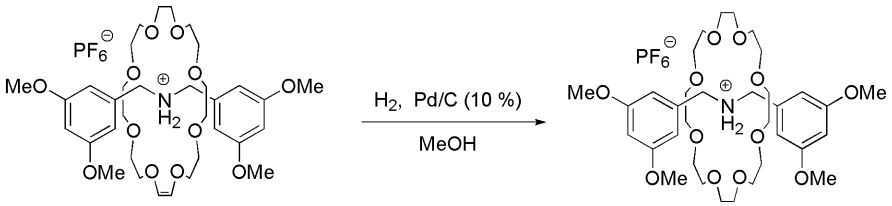
Characterization of [2]rotaxane **A2.8** by ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry (electrospray), and X-ray crystallographic analysis confirmed the interlocked nature of (Figure A2.1).

Figure A2.1. Molecular structure of [2]rotaxane **A2.8** (PF_6^- anion and hydrogen atoms omitted for clarity). Atoms are represented by thermal ellipsoids at 50% probability.



Grown from a mixture *E* and *Z* isomers, the structure of **A2.8** obtained by X-ray crystallography is derived almost entirely from the *E* isomer, although disorder in the structure suggests some *Z* isomer is present. Hydrogenation (H_2/Pd/C) of **A2.8** resulted in the saturated rotaxane **A2.9**, and resolved the spectroscopic ambiguity (Scheme A2.5).

Scheme A2.5. Hydrogenation of **A2.8**.

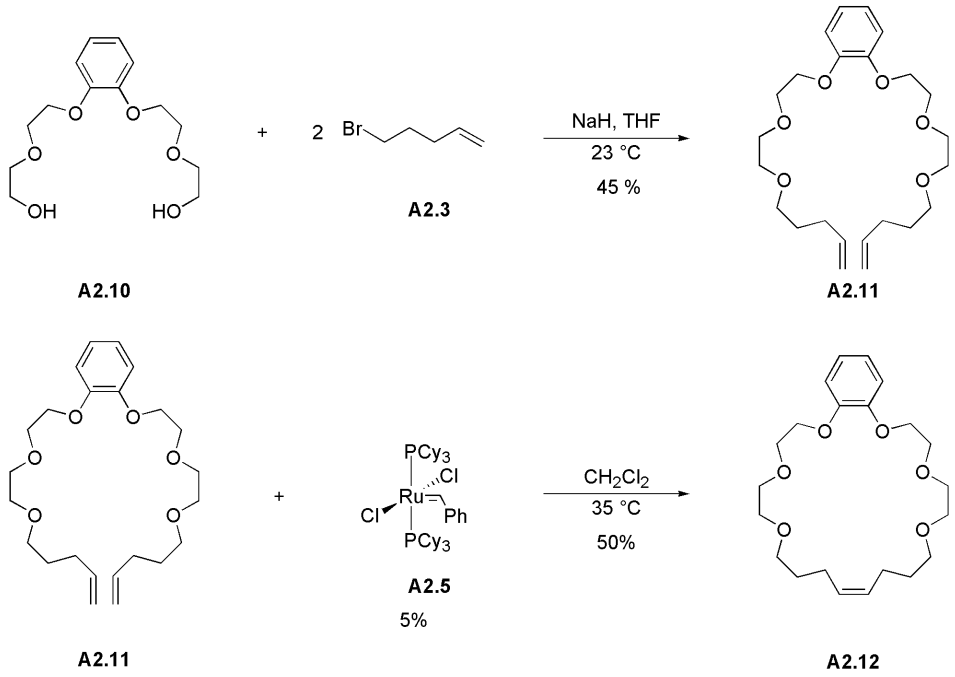


A2.8 **A2.9**

Derivatization of the crown ether, often desirable for the construction of extended supramolecular arrays, can be easily achieved by adding a benzo ring fused to the parent macrocycle (**A2.6**, Scheme A2.6).[13] Therefore, the benzo analogue of macrocycle **A2.6** was prepared (Scheme A2.6). Alkylation of known diol **A2.10**[14] with 5-bromo-1-pentene (**A2.3**) afforded diolefin **A2.11**, which was converted to the desired benzo-crown ether analogue **A2.12** via RCM mediated by Ru catalyst **A2.5**. The K_a value for the interaction between **A2.12** and dibenzylammonium hexaflourophosphate was shown to be ~10 M^{-1} (CD_3CN, 295 K), approximately one order of magnitude lower that that observed for **A2.6**. This decreased affinity for secondary ammonium ion binding is likely due to the reduced hydrogen bonding ability of the benzo-substituted macrocycle, as two of the O atom donors are now phenolic and, consequently, less basic. As in the case of the non-benzo macrocycle **A2.6**, hydrogenation of **A2.12** affords the saturated analogue, which

shows little change in the binding affinity for dibenzylammonium hexafluorophosphate (K_a ~10 M^{-1}).

Scheme A2.6. Synthesis of benzo-crown macrocycle **A2.12**.



Despite the decreased binding affinity, benzo-substituted rotaxane **A2.13** (*E*/*Z* mixture) was obtained in moderate yield in the RCM reaction of **A2.12** in the presence of end-capped dibenzylammonium hexafluorophosphate salt **A2.7** (Scheme A2.7). The yield of benzo[2]rotaxane **A2.13** was lower than that of non-benzo[2]rotaxane **A2.8** (30% vs. 73%). ^{1}H and ^{13}C NMR and mass spectroscopy, along with X-ray diffraction analysis, confirmed the structure of **A2.13** (Figure A2.2). The crystal structure of **A2.13** contains both *E* and *Z* isomers, which are present in an approximately 1:1 ratio.

Scheme A2.7. Synthesis of benzo-[2]rotaxane **A2.13**.

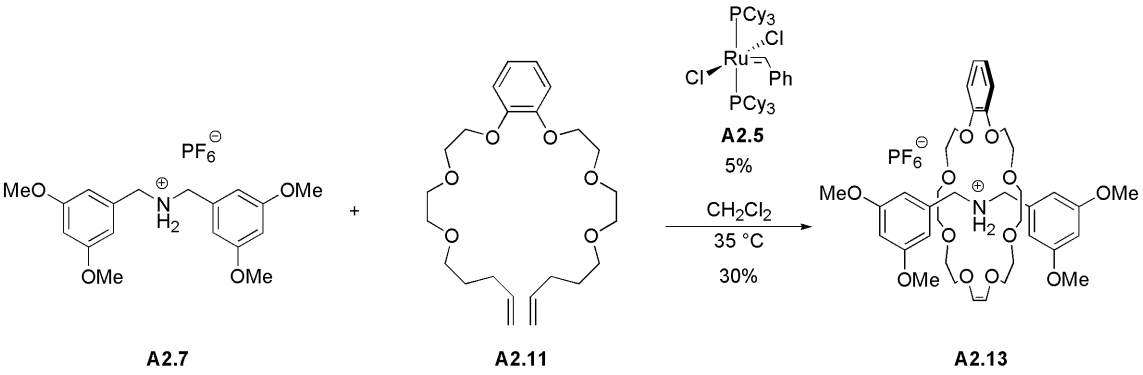
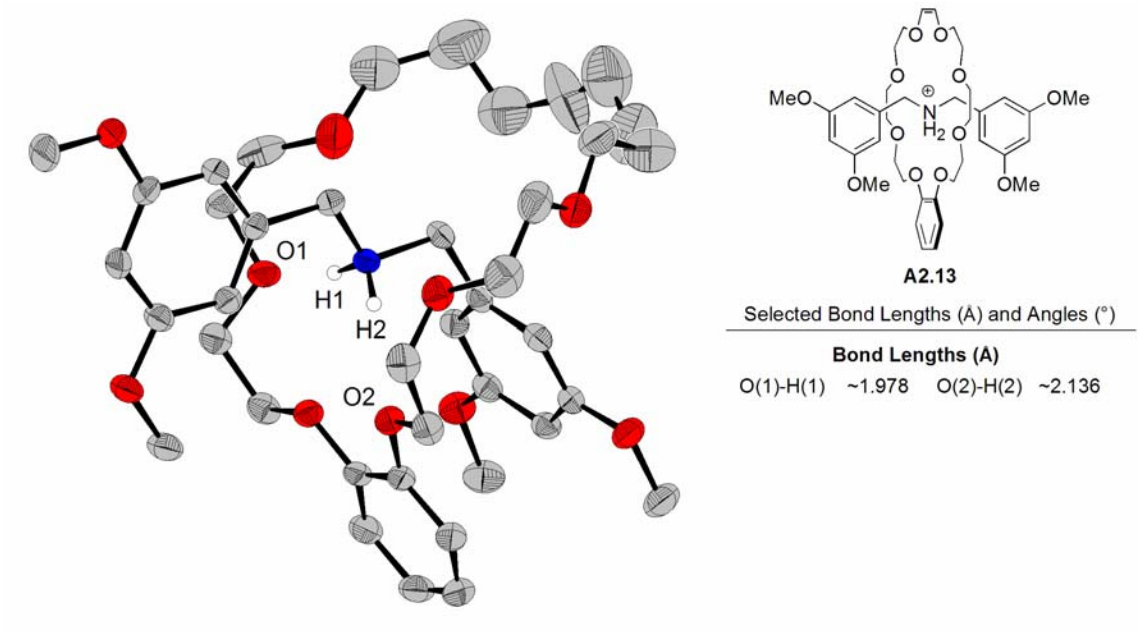


Figure A2.2. Molecular structure of benzo-[2]rotaxane **A2.13** (PF_6^- anion and hydrogen atoms omitted for clarity). Atoms are represented by thermal ellipsoids at 50% probability.



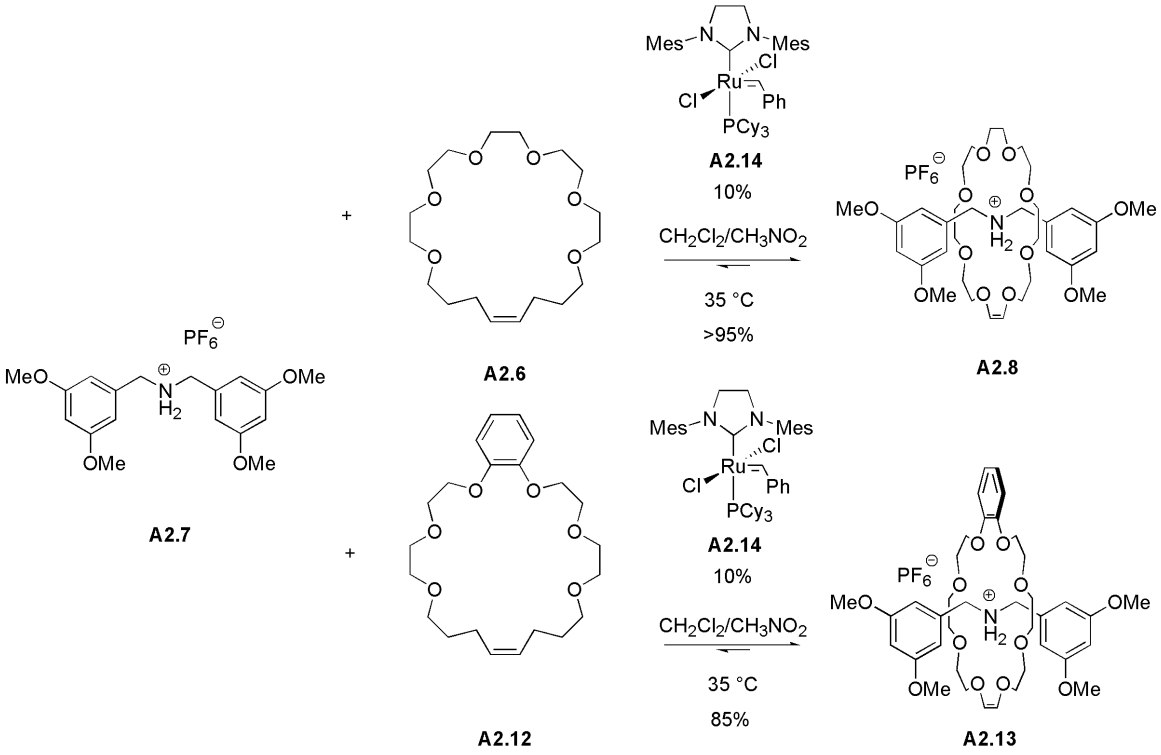
A2.4 "Magic Ring" Rotaxane Synthesis

To demonstrate that thermodynamic control of rotaxane formation is attainable through the use of olefin metathesis, a "magic ring" experiment was performed in which the rotaxane was assembled directly from its preformed components.[15] A CD_2Cl_2/CD_3NO_2 (80:20) solution containing equimolar quantities of crown ether **A2.6**

and dibenzylammonium salt **A2.7** was prepared (CD_3NO_2 is required to ensure complete dissolution of **A2.7**). Prior to catalyst addition, ^{1}H NMR spectroscopy revealed that the end-capped secondary ammonium ion **A2.7** did not pass through the cavity of the 24-membered macrocycle. However, upon addition of 10 mol% of ($IMesH_2$)(PCy_3)Cl_2Ru=CHPh (**A2.14**),[16] the system was able to reach a thermodynamic minimum (driven by the formation of N^+–H···O and C–H···O hydrogen bonds), resulting in the formation of [2]rotaxane **A2.8** (Scheme A2.8). ^{1}H NMR revealed that equilibrium (>95% interlocked species) was achieved in 45 min.

In an analogous fashion, the "magic ring" experiment was attempted with benzo-substituted macrocycle **A2.12**, with similar success (Scheme A2.8). In this case, equilibrium was reached in less time (~20 min), and afforded a lower yield of interlocked species (~85% yield of the benzo-[2]rotaxane **A2.13**), presumably reflecting the reduced binding affinity of macrocycle **A2.12** for secondary dibenzylammonium ions.

Scheme A2.8. The "magic ring" syntheses of [2]rotaxane **A2.8** and benzo-[2]rotaxane **A2.13**.



A2.5 Conclusion

Diolefin macrocyclic precursors have been shown to cyclize around an appropriately-substituted dibenzylammonium salt to produce corresponding [2]rotaxanes. Exploiting Ru-mediated olefin metathesis in this "clipping" procedure allows the process to occur under thermodynamic control. This dynamic feature allows the "magic ring" synthesis of mechanically-interlocked molecules, whereby exposure of the preformed components to the necessary catalytic agent causes the macrocycle to open and close repeatedly. This allows the system to reach a thermodynamically favored state.

Following the successful application of this methodology to the synthesis of simple [2]rotaxanes, the formation of a [2]catenane has been demonstrated,[17] and the

syntheses of more intricate interlocked molecular architectures, e.g., daisy-chains,[13] are currently being explored. In addition, the very high yields (for interlocked molecules) demonstrated in the reactions presented above suggest that the synthesis of polymers with novel interlocked architectures may also be attainable.

A2.6 Acknowledgments

The bulk of this research was performed by Andreas Kilbinger and Stuart Cantrill (I synthesized **A2.7**, performed the first rotaxane synthesis and assisted with characterization). The text of this chapter was adapted from a communication written by Stuart Cantrill.[18] X-ray crystallographic analyses of **A2.8** and **A2.13** were performed by Mike Day and Larry Henling. Mona Shahgholi performed mass spectral analysis.

A2.7 Experimental Details

All reagents were obtained from Aldrich and used without further purification. ^{1}H NMR spectra were recorded at 300 MHz (Varian Mercury), ^{13}C NMR were recorded at 75 MHz (Varian Mercury). Chemical shifts are quoted in parts per million (ppm) using residual protic solvent as the internal standard. Mass analysis was performed by electrospray ionization mass spectrometry using an ion trap mass spectrometer (LCQ Classic, ThermoFinnigan, CA). Solutions analyzed were approximately 1 μM in concentration and were prepared in 1:1 (v/v) acetonitrile: 0.1% acetic acid. Compounds **A2.5**,[9] **A2.7**,[12] **A2.10**,[14] **A2.14**,[16] and dibenzylammonium hexafluorophosphate,[19] were prepared following literature procedure. In cases where *E*/*Z* mixtures of products were obtained, the minor and the major isomers are, where possible, marked (mi) and (ma), respectively.

Pentaethylene glycol di-pent-4-enyl ether (**A2.4**). A solution of pentaethylene glycol (**A2.2**) (24.2 g, 100. mmol, 1.00 equiv) in THF (50 mL) was slowly added dropwise to a suspension of NaH (60% in oil, 12 g, 300 mmol, 5.0 equiv) in THF (50 mL). This

mixture was stirred at ambient temperature under an N_2 atmosphere until no further H_2 evolution was observed. The mixture was cooled with an ice bath and a solution of 5-bromopentene (**A2.3**) (45.3 g, 300. mmol, 3.00 equiv) and sodium iodide (1 g, 6 mmol) in THF (100 mL) was added dropwise. The reaction was stirred for 5 d under ambient conditions, and subsequently quenched with isopropanol, and then with water. All solvents were removed under reduced pressure and the residue purified by column chromatography (SiO_2, EtOAc) to give the desired product (19.0 g, 50.0%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44–1.54 (m, 4H), 1.88–1.98 (m, 4H), 3.28 (t, *J* = 6.5 Hz, 4H), 3.36–3.50 (m, 20H), 4.73–4.87 (m, 4H), 5.55–5.70 (m, 2H); ^{13}C NMR (75 Mhz, $CDCl_3$): δ = 28.4, 29.8, 69.6, 70.1, 114.1, 137.5 (the required number of peaks is not observed as a consequence of incidental overlap); MS (ESI): *m/z* (%): 375.0 $[M]^+$ (100).

1,2-Bis-[3,6-dioxa-undec-10-enoxy]benzene (**A2.11**). A solution of **A2.10** (3.80 g, 13.1 mmol, 1.00 equiv) in THF (30 mL) was slowly added dropwise to a suspension of NaH (60% in oil, 2.60 g, 65.5 mmol, 5.00 equiv) in THF (30 mL). This mixture was stirred at ambient temperature under an N_2 atmosphere until no further H_2 evolution was observed. The mixture was cooled with an ice bath and a solution of 5-bromopentene (**A2.3**) (5.90 g, 39.3 mmol, 3 equiv) in THF (30 mL) was added dropwise. The reaction was stirred for 5 d under ambient conditions, and subsequently quenched with isopropanol, then with water. All solvents were removed under reduced pressure and the residue purified by column chromatography (SiO_2, EtOAc) to give the desired product (2.5 g, 45%) as a colorless liquid. ^{1}H NMR (300 Mhz, $CDCl_3$): δ = 1.60–1.70 (m, 4H), 2.04–2.14 (m, 4H),

3.44 (t, *J* = 6.5 Hz, 4H), 3.53–3.59 (m, 4H), 3.66–3.72 (m, 4H), 3.80–3.86 (m, 4H), 4.89–5.02 (m, 4H), 5.70–5.86 (m, 2H), 6.82–6.92 (m, 4H); ^{13}C NMR (75 Mhz, $CDCl_3$): δ = 28.6, 30.1, 68.7, 69.5, 70.0, 70.4, 70.6, 114.4, 114.6, 121.3, 137.9, 148.6; MS (ESI): *m/z* (%): 423.0 $[M]^+$ (100).

1,4,7,10,13,16-Hexaoxa-cyclotetracos-20-ene (**A2.6**). $RuCl_2(=CHPh)(PCy_3)_2$ (**A2.5**) (200 mg, 5 mol%) was added to a degassed solution of **A2.4** (2.0 g, 5.3 mmol) in dichloromethane (1000 mL) and the mixture was heated under reflux for 24 hrs under an N_2 atmosphere. The solution was cooled down to room temperature, and ethylvinyl ether (1 mL) was added and the mixture stirred for 1 hr. The solvent was removed under reduced pressure and the crude oil was purified by column chromatography (SiO_2, EtOAc) to give the desired product as a mixture of *E* and *Z* isomers (0.9 g, 48%) as a pale yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52–1.64 (m, 4H), 1.99–2.13 (m, 4H), 3.38–3.45 (m, 4H), 3.50–3.57 (m, 4H), 3.58–3.66 (m, 16H), 5.29–5.39 (m, 2H); ^{13}C NMR (75 Mhz, $CDCl_3$): δ = 23.3 (mi), 28.4 (ma), 28.8 (ma), 29.2 (mi), 69.63, 69.69, 69.89, 70.16, 70.18, 70.24, 70.28, 70.32, 129.2 (mi), 129.7 (ma) (Major and minor peaks could not be distinguished in the region between δ = 69–71 ppm); MS (ESI): *m/z* (%): 347.1 $[M+H]^+$ (100).

Unsaturated-Benzo Crown (**A2.12**). $RuCl_2(=CHPh)(PCy_3)_2$ (**A2.5**) (100 mg, 5 mol%) was added to a degassed solution of **A2.11** (1.0 g, 2.4 mmol) in dichloromethane (500 mL) and the mixture was heated under reflux for 24 hrs under an N_2 atmosphere. The solution was cooled down to room temperature, and ethylvinyl ether (1 mL) was added

and the mixture stirred for 1 hr. The solvent was removed under reduced pressure and the crude oil was purified by column chromatography (SiO_2, EtOAc) to give pure and mixed *E* and *Z* isomer fractions of the desired product (total: 470 mg, 50%) as pale yellow liquid. Isomer **a**: ^{1}H NMR (300 Mhz, $CDCl_3$): δ = 1.53–1.65 (m, 4H), 2.07–2.17 (m, 4H), 3.42 (t, *J* = 6.5 Hz, 4H), 3.53–3.59 (m, 4H), 3.73–3.79 (m, 4H), 3.83–3.89 (m, 4H), 4.10–4.16 (m, 4H), 5.27–5.38 (m, 2H), 6.86 (s, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 23.5, 29.3, 69.2, 69.7, 70.0, 70.2, 70.7, 114.3, 121.2, 129.5, 148.7; MS (ESI): *m/z* (%): 395.0 $[M+H]^+$ (100). Isomer **b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.57–1.68 (m, 4H), 2.01–2.10 (m, 4H), 3.44 (t, *J* = 6.5 Hz, 4H), 3.54–3.60 (m, 4H), 3.70–3.75 (m, 4H), 3.82–3.88 (m, 4H), 4.11–4.17 (m, 4H), 5.35–5.39 (m, 2H), 6.86 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.6, 28.8, 68.8, 69.5, 69.8, 70.0, 70.5, 114.2, 121.2, 130.1, 148.6; MS (ESI): *m/z* (%): 395.0 $[M+H]^+$ (100).

Non-Benzo-Crown Rotaxane (**A2.8**). $RuCl_2(=CHPh)(PCy_3)_2$ (**A2.5**) (200 mg, 5 mol%) was added to a degassed solution of **A2.4** (2.0 g, 5.3 mmol) and **A2.7** (2.4 g, 5.3 mmol) in dichloromethane (50 mL) and the mixture was heated under for 24 hrs under an N_2 atmosphere. The solution was cooled down to room temperature, and ethylvinyl ether (1 mL) was added and the mixture stirred for 1 hr. The dichloromethane solution was poured into diethyl ether (400 mL) and the precipitate was recovered by filtration. This solid was recrystallized from EtOAc to afford the desired compound (as an *E*/*Z* mixture) as colorless crystals (3.2 g, 73%). M.p. 126–129 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59–1.72 (m, 4H), 2.03–2.14 (m, 4H), 3.11–3.18 (m, 4H), 3.27–3.36 (m, 4H), 3.50–3.59 (m, 4H), 3.65–3.75 (m, 4H), 3.82 (s, 12H), 4.23–4.38 (m, 4H), 5.32–5.44 (m, 2H), 6.47–

6.51 (m, 2H), 6.59–6.65 (m, 4H), 7.82 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.4 (mi), 27.9 (ma), 28.2 (ma), 30.1 (mi), 52.1 (ma), 52.2 (mi), 55.5, 69.2, 69.5, 70.1, 70.2, 70.3, 70.5, 70.6, 71.1, 71.4, 71.5, 100.4, 107.8 (mi), 108.0 (ma), 129.3 (mi), 130.5 (ma), 132.7, 160.7 (ma), 160.8 (mi); MS (ESI): *m/z* (%): 364.5 $[M–PF_6]^+$ (100).

Benzo-Crown Rotaxane (**A2.13**). $RuCl_2(=CHPh)(PCy_3)_2$ (**A2.5**) (80 mg, 5.0 %) was added to a degassed solution of **A2.11** (800 mg, 1.9 mmol) and **A2.7** (850 mg, 1.9 mmol) in dichloromethane (50 mL) and the mixture was heated under for 24 hrs under an N_2 atmosphere. The solution was cooled down to room temperature, and ethylvinyl ether (1 mL) was added and the mixture stirred for 1 hr. The solvent was removed under reduced pressure and the crude oil was purified by column chromatography (SiO_2, EtOAc) to afford the desired compound (as an *E*/*Z* mixture) as a white solid (0.5 g, 30%), which could further be purified, if necessary, upon recrystallization from EtOAc. M.P. 162–163 °C; ^{1}H NMR (300 Mhz, $CDCl_3$): δ = 1.60–1.75 (m, 4H), 2.05–2.21 (m, 4H), 3.50–3.75 (m, 28H), 4.00–4.08 (m, 4H), 4.32–4.48 (m, 4H), 5.39–5.52 (m, 2H), 6.20–6.25 (m, 2H), 6.49–6.54 (m, 4H), 6.60–6.67 (m, 2H), 6.80–6.87 (m, 2H), 7.98 (br s, 2H); ^{13}C NMR (75 Mhz, $CDCl_3$): δ = 24.8 (mi), 27.9 (ma), 28.6 (ma), 30.3 (mi), 52.2, 55.2, 67.8, 68.2, 69.4, 69.6, 69.7, 70.0, 70.9, 71.2, 71.7, 71.8, 99.7 (mi), 99.9 (ma), 106.6 (mi), 106.9 (ma), 111.3 (mi), 111.4 (ma), 121.3, 129.4 (mi), 130.7 (ma), 132.3 (mi), 132.4 (ma), 145.6 (mi), 145.7 (ma), 160.7 (ma), 160.8 (mi); MS (ESI): *m/z* (%): 712.5 $[M–PF_6]^+$ (100).

Hydrogenation of A2.8: *Crown Ethers*: Pd/C (10 %) was added to a 0.2 M solution of [2]rotaxane **A2.8** in MeOH. A slight vacuum was applied to the reaction mixture until

boiling of the solvent was observed. The reaction vessel was flushed with H_2, introduced via a balloon, and the mixture stirred vigorously for 5 hrs under ambient conditions. Filtration and removal of solvent under reduced pressure gave the hydrogenated [2]rotaxane **A2.9** in good yield. The product was recrystallized from EtOAc to afford a white powder. M.p. 112–113 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30–1.60 (m, 12H), 3.14 (s, 4H), 3.28–3.33 (m, 4H), 3.48–3.72 (m, 16H), 3.82 (s, 12H), 4.29–4.36 (m, 4H), 6.50 (t, *J* = 2.0 Hz, 2H), 6.65 (d, *J* = 2.0 Hz, 4H), 7.88 (br s, 2H); ^{13}C NMR (75 Mhz, $CDCl_3$): δ = 25.3, 27.7 29.3, 52.5, 55.5, 70.0, 70.3, 70.5, 71.6, 100.6, 108.0, 132.7, 160.8 (the required number of peaks is not observed as a consequence of incidental overlap); MS (ESI): *m/z* (%): 666.4 $[M–PF_6]^+$ (100).

A2.8 References

[1] (a) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725–2828. (b) *Molecular Catenanes, Rotaxanes and Knots* (Eds.: J.-P. Sauvage, C. Dietrich-Buchecker), Wiley-VCH, Weinheim, **1999**.

[2] (a) Lehn, J.-M. *Chem. Eur. J.* **1999**, 2455–2463. (b) Rowan, S. J.; Cantrill, S. J.; Cousins, G. R. L.; Sanders, J. K. M.; Stoddart, F. *Angew. Chem. Int. Ed.* **2002**, *41*, 898–952.

[3] For recent examples of kinetically-controlled rotaxane syntheses, see: (a) Loeb, S. J.; Wisner, J. A. *Chem. Commun.* **2000**, 845–846. (b) Reuter, C.; Vögtle, F. *Org. Lett.* **2000**, *2*, 593–595. (c) Buston, J. E. H.; Marken, F.; Anderson, H. L. *Chem. Commun.* **2001**, 1046–1047. (d) Chiu, S.-H.; Rowan, S. J.; Cantrill, S. J.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **2002**, *8*, 5170–5183.

[4] For the earliest reported examples of a rotaxane synthesis that utilizes reversible covalent bond formation, see: Harrison, I. T. *J. Chem. Soc. Chem. Commun.* **1972**, 231–232.

[5] Certain kinetically-labile metal-ligand interactions have also been exploited as the reversible "reaction" step in the formation of dynamic (organometallic) rotaxanes, see: a) Baer, A. J.; Macartney, D. H. *Inorg. Chem.* **2000**, *39*, 1410–1417. (b) Chichak, K.; Walsh, M. C.; Branda, N. R. *Chem. Commun.* **2000**, 847–848. (c) Gunter, M. J.; Bampos, N.; Johnstone, K. D.; Sanders, J. K. M. *New J. Chem.* **2001**, *25*, 166–173. (d) Chang, S.-Y.; Choi, J. S.; Jeong, K.-S. *Chem. Eur. J.* **2001**, *7*, 2687–2697. (e) Hunter, C.A.; Low, C. M. R.; Packer, M. J.; Spey, S. E.; Vinter, J. G.; Vysotsky, M. O.; Zonta, C. *Angew. Chem. Int. Ed.* **2001**, *40*, 2678–2682. Imine: a) Cantrill, S. J.; Rowan, S. J.;

Stoddart, J. F. *Org. Lett.* **1999**, *1*, 1363–1366. (b) Rowan, S. J.; Stoddart, J. F. *Org. Lett.* **1999**, *1*, 1913–1916. (c) Glink, P. T.; Olivia, A. I.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem. Int. Ed.* **2001**, *40*, 1870–1875. (d) Leigh, D. A.; Lusby, P. J.; Teat, S. J.; Wilson, A. J.; Wong, J. K. Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 1538–1543. Disulfide: a) Kolchinski, A. G.; Alcock, N. W.; Roesner, R. A.; Busch, D. H. *Chem. Commun.* **1998**, 1437–1438. (b) Furusho, Y.; Hasegawa, T.; Tsuboi, A.; Kihara, N.; Takata, T. *Chem. Lett.* **2000**, 18–19. (c) Oku, T.; Furusho, Y.; Takata, T. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 119–123.

[6] (a) Kidd, T. J.; Leigh, D. A.; Wilson, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 1599–1600. Ring closing olefin metathesis has also been applied to catenane syntheses wherein the reversibility of the systems could not be demonstrated or was not investigated, see: (b) Hamilton, D. G.; Feeder, N.; Teat, S. J.; Sanders, J. K. M. *New J. Chem.* **1998**, 1019–1021. (c) Weck, M.; Mohr, B.; Sauvage, J.-P.; Grubbs, R. H. *J. Org. Chem.* **1999**, *64*, 5463–5471.

[7] Wisner, J. A.; Beer, P. D.; Drew, M. G. B.; Sambrook, R. *J. Am. Chem. Soc.* **2002**, *124*, 12469–12476.

[8] (a) Kolchinski, A. G.; Busch, D. H.; Alcock, N. W. *J. Chem. Soc. Chem. Commun.* **1995**, 1289–1291. (b) Cantrill, S. J.; Pease, A. R.; Stoddart, J. F. *J. Chem. Soc. Dalton Trans.* **2000**, 3715–3734 and references therein. (c) Cantrill, S. J.; Fulton, D. A.; Heiss, M.; Pease, A. R.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **2000**, *6*, 2274–2287.

[9] a) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc*. **1996**, *118*, 100–110. (b) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **1995**, *34*, 2039–2041.

[10] Single-point method, see: Adrian, J. C.; Wilcox, C. S. *J. Am. Chem. Soc.* **1991**, *113*, 678–680. It should be noted that, in this case, the K_a value reflects a total association constant, combining the contributions from both the *cis* and *trans* isomers of the crown ether present in solution.

[11] Ashton, P. R.; Bartsch, R. A.; Cantrill, S. J.; Hanes, Jr., R. E.; Hickingbottom, S. K.; Lowe, J. N.; Preece, J. A.; Stoddart, J. F.; Talanov, V. S.; Wang, Z.-H. *Tetrahedron Lett.* **1999**, *40*, 3661–3664.

[12] Cantrill, S. J.; Fyfe, M. C. T.; Heiss, A. M.; Stoddart, J. F.; White, A. J. P. Williams, D. J. *Org. Lett.* **2000**, *2*, 61–64.

[13] Cantrill, S. J.; Youn, G. J.; Stoddart, J. F.; Williams, D. J. *J. Org. Chem.* **2001**, *66*, 6857–6872.

[14] Colonna, B.; Echegoyen, L. *Chem. Commun*. **2001**, 1104–1105.

[15] The term “magic ring” refers to the nature of the reaction, in that an already cyclized macrocycle is transformed into an interlocked molecule, similar to a magician’s trick.

[16] [$IMesH_2$ = 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene], see: Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956.

[17] Guidry, E. N.; Cantrill, S. J.; Stoddart, J. F.; Grubbs, R. H. *Org. Lett.* **2005**, *7*, 2129–2132.

[18] Kilbinger, A. F. M.; Cantrill, S. J.; Waltman, A. W.; Day, M. W.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 3281–3285.

[19] Ashton, P. R.; Chrystal, E. J. T.; Glink, P. T.; Menzer, S.; Schiavo, C.; Spencer, N.; Stoddart, J. F.;Tasker, P. A.; White, A J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 709–728.