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Selective Synthesis of [2]- and [3]Catenane Tuned by Ring Size and Concentration

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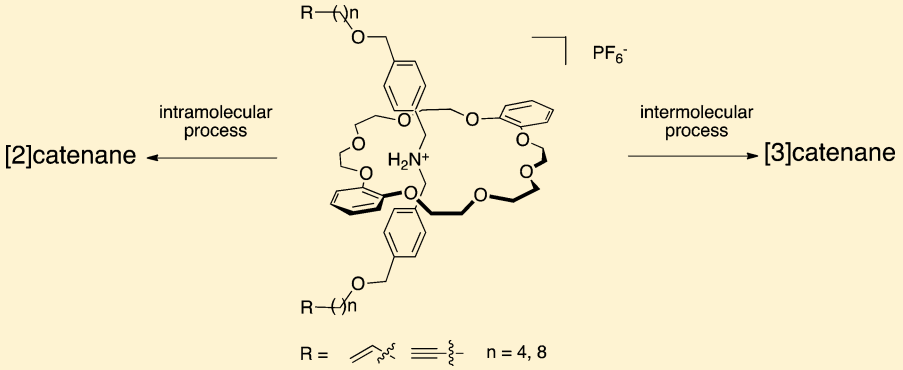
Supporting Information



ABSTRACT: The syntheses of [2]- and [3]catenanes by olefin metathesis and oxidative acetylide coupling have been studied in detail. Pseudorotaxanes that were obtained by mixing crown ether and ammonium salts containing two terminal reactive end-groups were converted to [2]- and [3]catenane. Their yields were influenced not only by the chain length of the ammonium salts but also by the concentration of the crown ether and the ammonium salts. The strain energies of [2]catenane were responsible for the formation of [2]catenane.

INTRODUCTION

Catenanes, which consist of two or more interlocked macrocycles, are of great interest in the field of supramolecular chemistry.[1] The macrocycles are not covalently connected but are linked by mechanical bonds. The mechanical bonds result in a unique molecular motion of the catenanes in which the macrocycles rotate around one another and change their spatial relationship to each other. This motion does not occur in molecules formed by covalent bonds, suggesting the potential for the application of catenanes in new materials and nanoscale molecular devices.[2] The synthesis of catenanes has been extensively studied, and sophisticated molecular devices based on catenanes have been developed.

One of the general synthetic strategies for catenanes is that a linear molecule threads into a macrocycle to form a pseudorotaxane, and the linear molecule is then cyclized to form a new macrocycle. Using this strategy, the first catenane was synthesized by Wasserman in 1960.[3] In that report, acyloin condensation of a diester in the presence of a macrocycle that had no specific interaction with the diester and statistically formed a pseudorotaxane with the diester yielded catenane in only 0.0001% yield. Statistical approaches have been inefficient. Therefore, rational and strategic approaches are necessary for the synthesis of catenanes. Three key steps are involved in this strategy. First, a linear molecule is threaded into a macrocycle. Second, the linear molecule is cyclized while maintaining the structure in which the linear molecule is threaded into the macrocycle. Last, the competing intra- or intermolecular reactions, which can be a potential challenge for the cyclization process, are controlled. To obtain catenanes, these three crucial steps must be performed.

Host–guest chemistry provides clever solutions for threading a linear molecule into a macrocycle without using statistical threading. In 1989, Stoddard developed pseudorotaxanes promoted by donor–acceptor interactions between electron-rich aromatics and paraquats to afford catenanes.[4] Since this pioneering work, many intermolecular forces, such as hydrogen bonding interactions,[5] donor–acceptor interactions,[6] and hydrophobic interactions[1d,7] between the linear molecule and the macrocycle, have been employed in the formation of pseudorotaxanes to form catenanes (e.g., crown ethers and ammonium salts, cyclodextrins and biphenyl, and cyclic tetraamides and amides). Metal coordination, another method for synthesizing pseudorotaxane, was first used in catenane synthesis by Dietrich–Buchecker and Sauvage in 1983.[8] The metal coordination process results in the formation of more stable pseudorotaxanes compared to the weak intermolecular interactions. Since stable pseudorotaxanes

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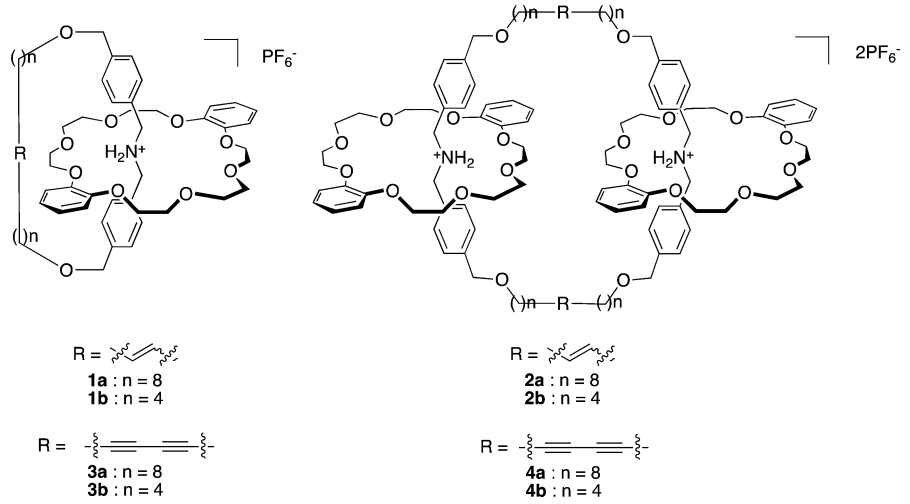

Figure 1. [2]Catenanes (**1a,b**, **3a,b**) and [3]catenanes (**2a,b**, **4a,b**).

permit the use of a variety of reaction conditions for macrocyclization, metal coordination is a favorable method for catenane synthesis.[9] In addition, the formation of stable pseudorotaxanes from low concentrations of each component, linear molecule and macrocycle, is advantageous for intramolecular cyclization. Complexations between Cu^{+} and phenanthroline-based ligands, Ru^{2+} and terpyridyl ligands, and Pd(II) and pyridyl ligands can also be effective for catenane synthesis.

Reaction conditions keeping pseudorotaxane formed by weak interactions or metal coordination are necessary for catenane synthesis. Alkene metathesis[9c,g,10a−i] is one of the most successful reactions for catenane synthesis. Olefin metathesis reactions occur under neutral conditions and near room temperature. These mild conditions prevent the dissociation of the host−guest complex and the decomposition of the coordination bond. Oxidative acetylide coupling of two terminal alkynes,[11] condensation of amines with acid chlorides,[12] imine formation/reductive amination,[13] quaternization of aromatic amines,[14] Williamson ether synthesis,[15] and the Huisgen reaction[16] are also employed in the cyclization process.

The presence of competitive intra- or intermolecular reactions is a fundamental and inevitable issue in the synthesis of macrocycles.[17] The synthesis of catenanes, including the macrocyclization process, may also be subject to this potential problem. In general, a lower concentration of substrate for macrocyclization results in intramolecular reactions to yield cyclic products, while a higher concentration facilitates intermolecular reactions to yield dimers, trimers, and oligomers. Although the intramolecular cyclization of pseudorotaxanes under lower concentrations appears to afford catenanes in good yield, lower pseudorotaxane concentrations result in their dissociation, particularly for pseudorotaxanes formed via weak intermolecular interaction, resulting in a low yield of catenanes. The concentrations of substrates influence not only the selectivity of the intra- or intermolecular reaction but also the stability of the pseudorotaxanes, yielding opposing effects.

We have previously reported the synthesis of catenanes composed of a crown ether and ammonium salts using olefin metathesis.[18] The selectivity of [2]- and [3]catenanes is influenced not only by the concentrations of the crown ether and ammonium salts but also by the length of the ammonium salts. Although several studies have investigated the selectivities of [2]- and [3]catenanes,[19] no relationships between the concentrations of the substrates and the selectivities of [2]- and [3]catenanes have been described. In the course of our study, oxidative acetylide coupling was applied to the selective synthesis of catenanes. Herein, we provide a detailed description of the selective synthesis of [2]- and [3]catenanes via olefin metathesis and oxidative acetylide coupling controlled by the concentration of the crown ether and the ammonium salts as well as the length of the ammonium salts (Figure 1).

RESULTS AND DISCUSSION

Synthesis of Ammonium Salts. The syntheses of ammonium salts **9a−b**, which are the precursors for olefin metathesis, and **9c−d**, which are the precursors for the oxidative acetylide coupling, are shown in Scheme 1. Etherification of diol **5**[20] with NaH and tosylate **6a−d** in DMF yielded **7a−d**. The deprotection of the BOC group with TFA afforded secondary amine **8a−d**. Treatment with hydrochloric acid followed by anion exchange from the chloride to the hexafluorophosphate yielded **9a−d**.

Determination of the Association Constants for Crown Ether−Ammonium Salt Complexation. To study the binding behavior of ammonium salt **9a** and dibenzo[24]crown-8 (DB24C) (**10**), a standard titration experiment was performed using ^{1}H NMR spectroscopy at room temperature in dichloromethane-d_2 (Figure 2). Simple mixing of the compounds yielded well-resolved signals resulting from the free and bound states, whose equilibrium was in slow exchange on the NMR time scale. Methylene protons H_i adjacent to the ammonium moiety shifted downfield, whereas upfield shifts were observed for aromatic protons H_g and H_h and methylene protons H_e and H_f adjacent to the ether oxygen, suggesting that these protons were shielded by the two aromatic rings connected to the crown ring. All of the protons on the crown ether were shifted upfield. These chemical shift changes are evidence of the formation of a pseudorotaxane composed of **9a** and **10** in which NH^{+}−O interactions and $\pi-\pi$ interactions between the secondary ammonium salt and the crown ether cooperatively stabilize the complex.[21] Signals of the free state of **9a** are slightly shifted compared with those of standard ^{1}H NMR spectra of **9a**. It is probably due to the face-to-face interaction between **9a** and **10**. Proton H_f at several concentrations of **9a** and **10** was integrated in the free and bound states, and the binding constant (K_a) of the host−guest complex was determined to be 4,700 ± 900 L mol^{-1} based on their ratio.[22]

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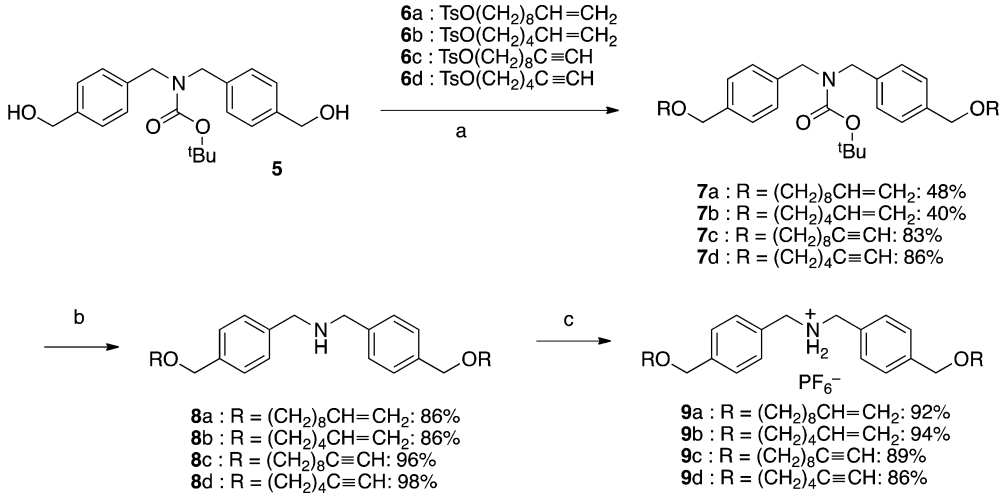
Scheme 1[a]



[a]Reagents and conditions: (a) **5**, NaH, DMF; (b) TFA, CH_2Cl_2; (c) 6 M HCl, acetone, then NH_4PF_6, CH_2Cl_2, acetone.

The association constants between **9a–d** and **10** are summarized in Table 1. In all cases, signals resulting from the free and bound states were observed. The exchange rate of the free and bound states was slower than the NMR time scale, regardless of the chain length of the ammonium salts. The length of the ammonium salt as well as terminal functional groups, double bonds, and triple bonds do not play an important role in the stability of crown-ammonium salt complexes. The obtained association constants suggest that the pseudorotaxanes should be formed on a millimolar scale.

Synthesis of Catenanes. Catenanes were synthesized by olefin metathesis according to Scheme 2(a). The treatment of pseudorotaxane **9a·10** derived from mixing DB24C **10** (0.002 M) and an ammonium salt containing two terminal olefin **9a** (0.002 M) in dichloromethane with 10 mol % of the first-generation Grubbs catalyst[23] yielded catenation products with undefined oligomeric byproducts. The catenation products were purified by column chromatography and gel permeation chromatography (GPC). [2]Catenane **1a** and [3]catenane **2a** were obtained in 56% and 2% yields. For the short ammonium salt **9b**, the same conditions yielded only [3]catenane **2b** in 25% yield.

The synthesis of catenane by oxidative acetylide coupling was performed according to Scheme 2(b). The treatment of pseudorotaxane **9c·10** derived from mixing DB24C **10** (0.002 M) and an ammonium salt containing two terminal C–C triple bonds **9c** (0.002 M) in dichloromethane with 3 equiv of $Cu(OAc)_2$ and 1 equiv of pyridine yielded catenation products with undefined oligomeric byproducts. The catenation products were purified by column chromatography and GPC. [2]Catenane **3a** and [3]catenane **4a** were obtained in 23% and 4% yields. For the short ammonium salt **9d**, the same conditions yielded [2]catenane **3b** and [3]catenane **4b** in 4% and 6% yields.

Mass Spectrometry and NMR Studies of Catenanes. The [2]- and [3]catenanes were characterized by ESI mass spectrometry. The positive ESI mass spectra of [2]catenane **1a**, [3]catenane **2a**, and [3]catenane **2b** are provided in Figure 3, and the positive ESI mass spectra of [2]catenane **3a**, [3]catenane **4a**, [2]catenane **3b**, and [3]catenane **4b** are provided in Figure 4. [2]Catenane **1a** exhibited signals corresponding to singly positively charged ions resulting from the loss of one hexafluorophosphate ion. However, [3]catenanes produced signals corresponding to doubly charged ions resulting from the loss of two hexafluorophosphate ions. These observed isotopic distributions were similar to the theoretical ones. These results suggest a structure in which the ammonium salts and the crown ethers are mechanically interlocked with each other. The number of ion charges indicates the number of macrocycles present in the obtained compounds.

The ^{1}H NMR spectra of [2]- and [3]catenanes obtained from olefin metathesis are shown in Figure 5. Olefin metathesis usually yields a mixture of alkene structural isomers. Therefore, NMR studies of mixtures of the *E*- and *Z*-isomers of catenanes were performed. The ^{1}H NMR signal of the vinylic protons was observed at approximately 5.4 ppm. In [3]catenane **2b**, two sets of signals for the vinylic protons were observed. The *E*- and *Z*-isomers were most likely obtained in the synthesis of the catenanes, but the *E*/*Z* ratio was not determined. For [3]catenane **2a**, the broadened signals of the vinylic protons also suggested a mixture of *E*- and *Z*-isomers. The mixtures of *E*- and *Z*-isomers are consistent with the broadened signals of the allylic protons, which are observed at approximately 2.0 ppm. The signals observed for the vinylic protons of [2]catenane **1a** appear to be a single set. Therefore, one isomer was obtained as a major product in the reaction. Although the spectra were nearly identical, slight differences were observed. The vinylic and allylic protons of [2]catenane **1a** were shifted upfield relative to those of [3]catenane **2a**, and the aromatic protons of the ammonium macrocycle of [2]catenane **1a**, which were observed in the range of 7.1–7.3 ppm, were shifted downfield relative to those of [3]catenane **2a**. These results suggest that the smaller ammonium macrocycle of [2]catenane **1a** is more strongly influenced by the crown ether than the larger diammonium macrocycle of [3]catenane **2a**.

The ^{1}H NMR spectra of [2]- and [3]catenanes obtained from oxidative acetylide coupling are shown in Figure 6. In contrast to the results of olefin metathesis, all of the signals clearly correspond to a single isomer. Although the spectra are nearly identical, slight differences were observed. The propargylic protons of [2]catenanes **3a** and **3b**, which were observed at approximately 2.2 ppm, were shifted upfield relative to those of [3]catenanes **4a** and **4b**, and the aromatic protons of the ammonium macrocycle of [2]catenanes **3a** and **3b**, which were observed in the range of 7.1–7.3 ppm, were shifted downfield relative to those of [3]catenanes **4a** and **4b**. These trends were

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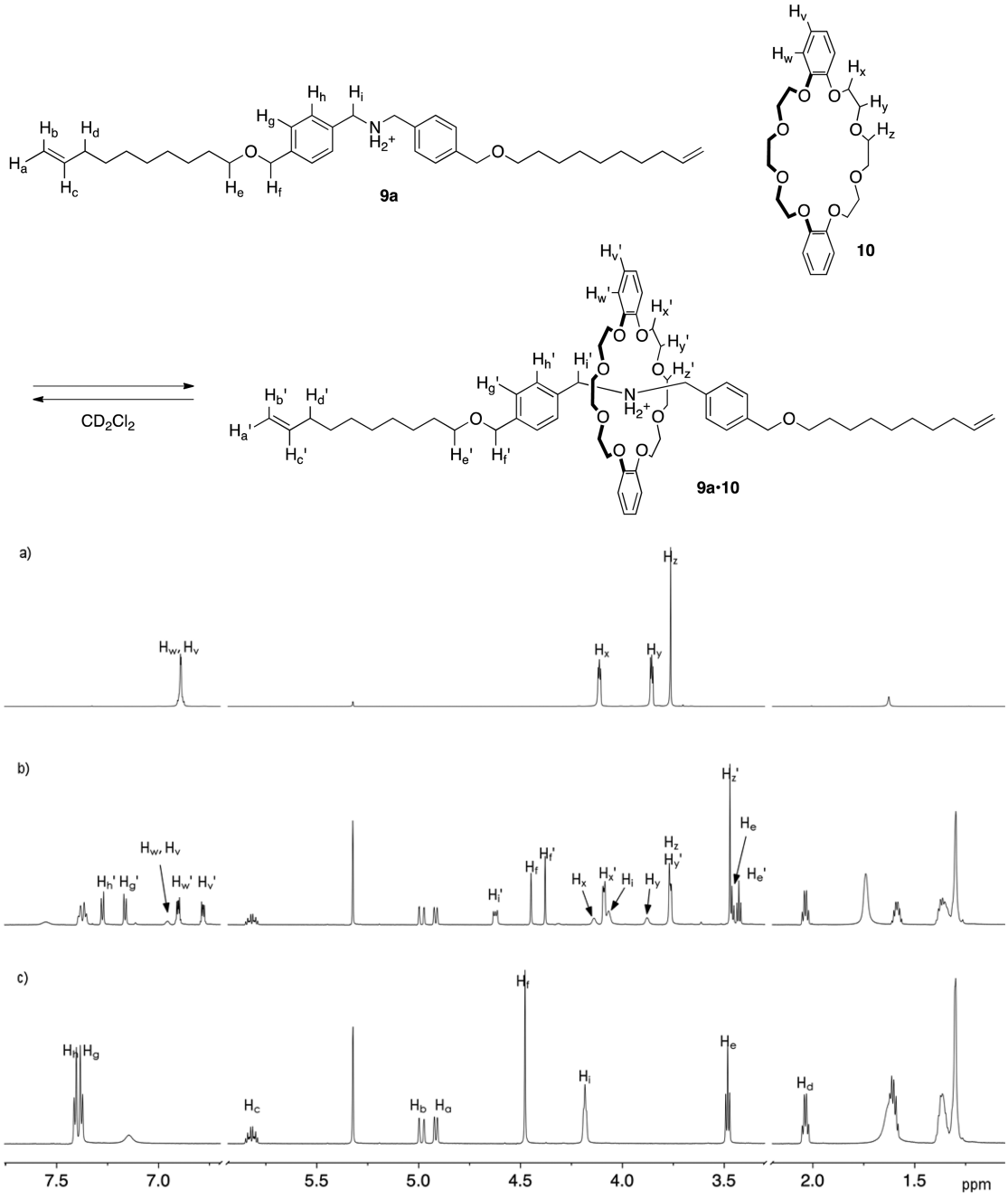

Figure 2. Partial ^{1}H NMR spectra (700 MHz) in CD_2Cl_2 at 23 °C of (a) DB24C **10**, (b) **10** (1.70×10^{-3} mol L^{-1}) + ammonium salt **9a** (1.29×10^{-3} mol L^{-1}), and (c) **9a**.

Table 1. Association Constants[a] (K_a/L mol^{-1}) for the Host–Guest Complexation of Ammonium Salts 9a–d with Crown Ether 10 in Dichloromethane-d_2 at 298 K

ammonium salt	association constants K_a [L mol^{-1}]
9a	4700 ± 900
9b	5800 ± 700
9c	8600 ± 800
9d	6100 ± 400

[a]Mixtures of **9a–d** ($1.56–3.92 \times 10^{-3}$ M) and **10** ($1.27–2.72 \times 10^{-3}$ M) were used for the association constants.

similar to those observed for olefin metathesis. In particular, the signals of [2]catenane **3b**, which contains a shorter ammonium macrocycle, were shifted more than those of [2]catenane **3a**, which contains a longer ammonium macrocycle. These results suggest that the smaller ammonium macrocycle of **3b** is more influenced by the crown ether than the longer ammonium macrocycle of **3a**.

Concentration Dependence of the [2]- and [3]Catenane Selectivity. Catenane synthesis is significantly influenced by the concentration of the substrate. As the pseudorotaxane concentration decreases, the pseudorotaxane undergoes an intramolecular reaction to yield [2]catenanes. However, pseudorotaxane can dissociate and reduce the yield of [2]catenanes. As the pseudorotaxane concentration increases, the pseudorotaxane undergoes an intermolecular reaction to afford [3]catenanes. However, the formation of other products, such as oligomeric linear molecules and catenanes with more than three rings, via the intermolecular reaction is also increased.

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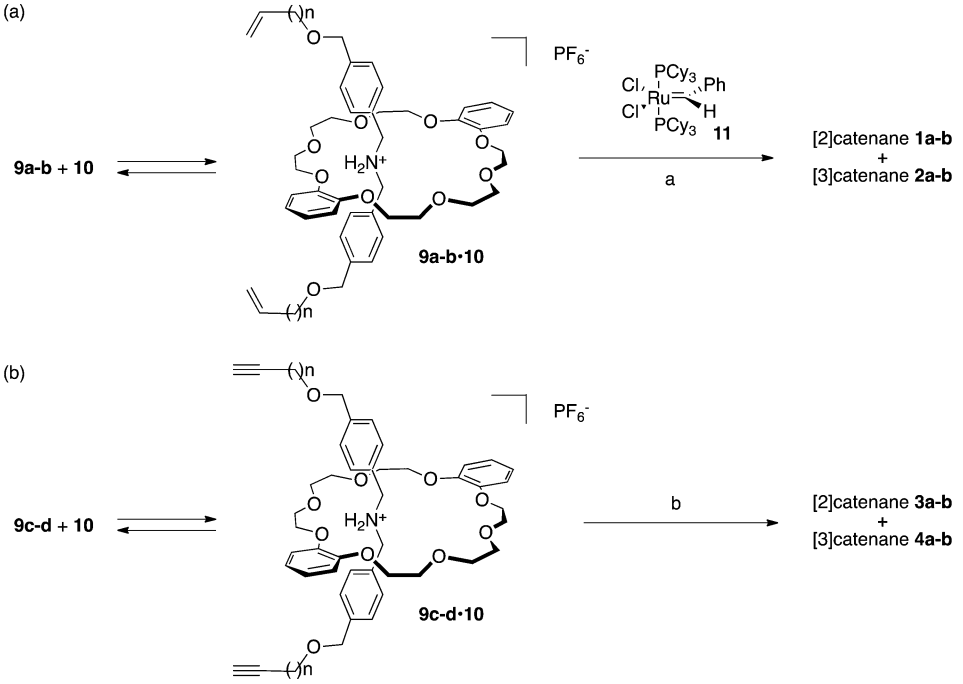
Scheme 2. Syntheses of Catenanes[a]



[a]Reagents and conditions: (a) first-generation Grubbs catalyst **11**, CH_2Cl_2, reflux; (b) $Cu(OAc)_2$, pyridine, CH_2Cl_2, reflux.

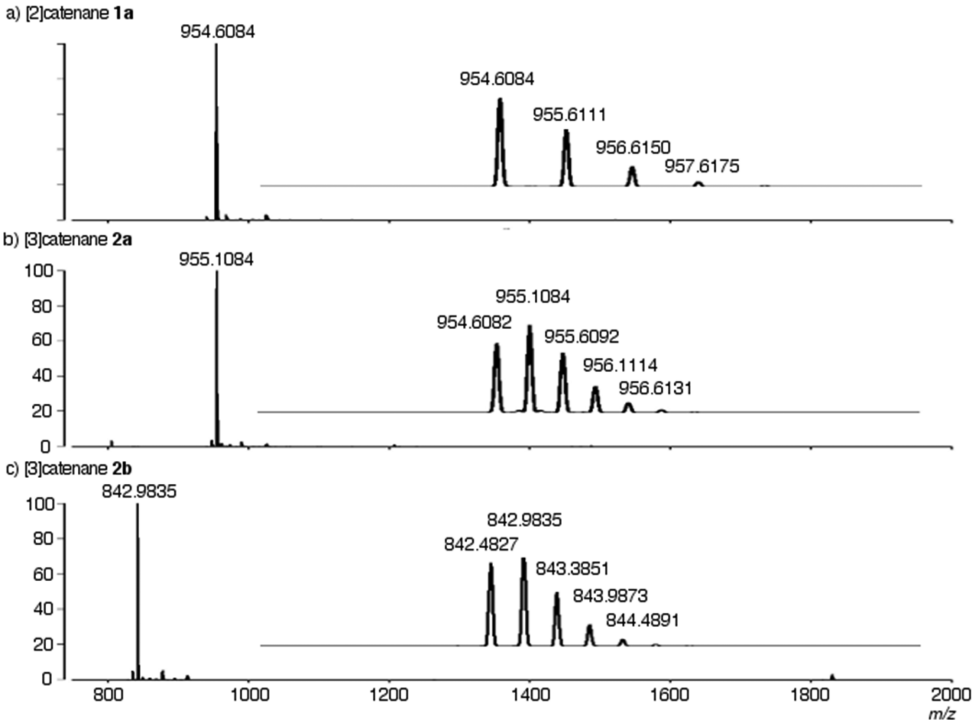


Figure 3. Positive ESI mass spectra of (a) [2]catenane **1a**, (b) [3]catenane **2a**, and (c) [3]catenane **2b**.

To investigate the concentration dependence of the substrates, olefin metathesis was performed under various concentrations of crown ethers and ammonium salts (Table 2). When the concentration of **9a** and **10** was 0.002 M in a dichloromethane solution, [2]catenane **1a** was obtained in 56% yield, and [3]catenane **2a** was obtained in 2% yield. By increasing the substrate concentrations, the yield of [3]-catenane **2a** increased, while that of [2]catenane **1a** decreased. Variation in the concentration of short ammonium salt **9b** yielded only [3]catenane **2b** under any of the tested concentration conditions.

When the concentrations of ammonium salt **9a** and crown ether **10** were 0.002, 0.01, and 0.02 M, 73%, 86%, and 90% of **9a** and **10** were estimated to form the pseudorotaxane **9a·10** based on the determined K_a. Therefore, if these statistical distributions influence the products, all of the reaction conditions should sufficiently yield catenation products. In fact, the total yields of the obtained catenanes were 58, 57, and 51%. Although the

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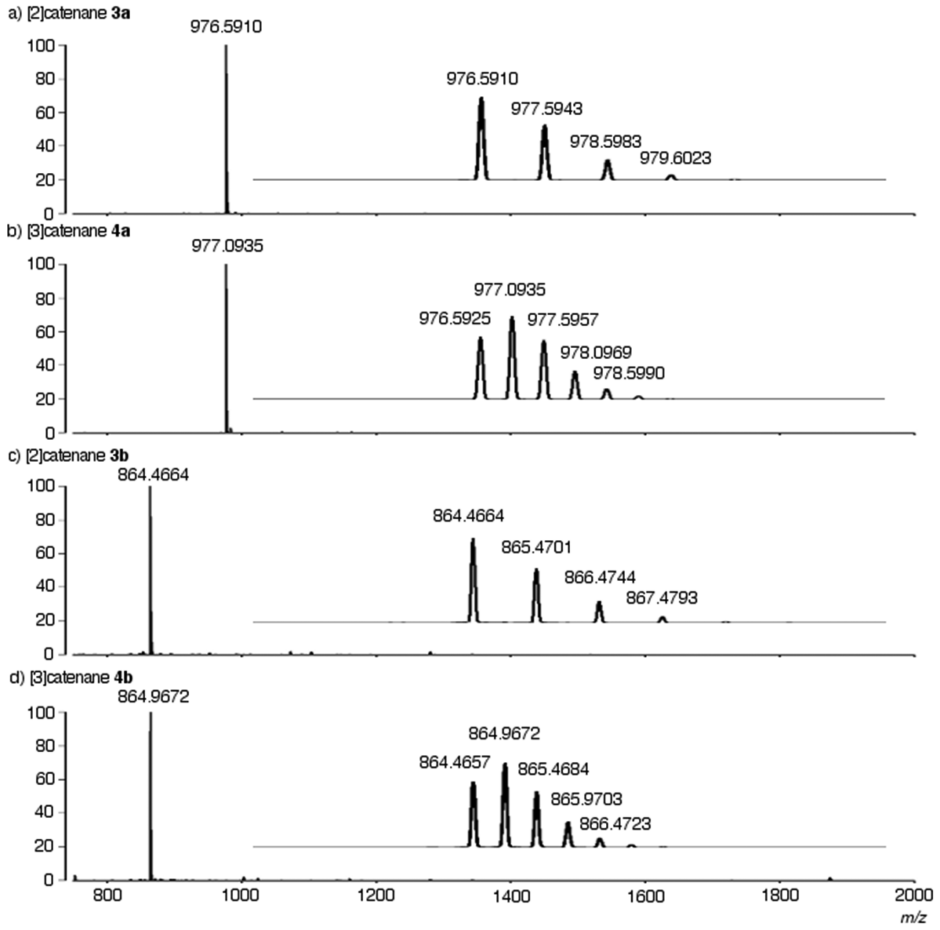

Figure 4. Positive ESI mass spectra of (a) [2]catenane **3a**, (b) [3]catenane **4a**, (c) [2]catenane **3b**, and (d) [3]catenane **4b**.

dynamic equilibrium for the formation of pseudorotaxane is attainable during the reaction, the static stability of the pseudorotaxane plays an important, determining role in catenane formation.

The concentration of pseudorotaxane **9a·10** influences the selectivity of the intra- or intermolecular reaction. The cyclization of **9a·10** is an intramolecular process that produces [2]catenane **1a**, whereas the intermolecular metathesis of **9a·10** followed by intramolecular metathesis yields [3]catenane **2a**. Although the formation of [3]catenanes involves an intramolecular process in the final step, the ratios of [2]catenanes to [3]catenanes may indicate the relative rate of the intra- and intermolecular processes in the cyclization reaction of **9a·10**.[24] The ratio at the lowest concentration (0.002 M) was the largest (i.e., 28) observed in the reactions of **9a** and **10**, suggesting that the intramolecular process is preferred over the intermolecular process. As the substrate concentrations increased, the ratio decreased. The intermolecular process is favored over the intramolecular processes as the concentration of pseudorotaxane **9a·10** increases. However, the ratio of [2]catenanes to [3]catenanes is greater than 1.0 for a concentration range of 0.002 to 0.02 M, and the intramolecular process most likely dominates under these conditions.

No [2]catenane **1b** was detected under any of the studied conditions. At a range of concentrations (i.e., 0.002, 0.01, and 0.02 M), only [3]catenane **2b** was obtained, in 25%, 33%, and 35% yield. In comparison to using ammonium salt **1a**, the intermolecular process was preferred over the intramolecular processes in the concentration range studied. The crown ether moiety could interfere with the intramolecular cyclization of pseudorotaxane **9b·10** due to the short length of the ammonium salt. **9b·10** most likely underwent an intermolecular reaction to yield [3]catenane **2b**, or it could have dethreaded followed by intramolecular cyclization to afford an ammonium macrocycle without a crown ether. The yield increased as the concentration of pseudorotaxane **9b·10** increased, suggesting that the formation of [3]catenane was preferred over the intermolecular cyclization involving dethreading of the ammonium salt at high concentrations.

Table 3 shows the yields of [2]- and [3]catenanes obtained from oxidative acetylide coupling at several concentrations of crown ethers and ammonium salts. When the concentration of **9c** and **10** was 0.002 M in a dichloromethane solution, [2]catenane **3a** was obtained in 23% yield, and [3]catenane **4a** was obtained in 4% yield. By increasing the concentrations to 0.01 M, the yield of [3]catenane **4a** increased, but the yield of [2]catenane **3a** slightly decreased. For short ammonium salt **9d**, the yield of [3]catenane **4b** was higher than that of [2]catenane **3b** under any of the concentrations tested.

In comparison to olefin metathesis, the total yields of the catenation products were lower under all of the reaction conditions. The association constants (K_a) between **9c**,**d** and **10** were nearly equal to those of **9a**,**b**. The static stabilities of pseudorotaxane most likely exhibited the same trends as in the olefin metathesis reaction. However, in the presence of pyridine, the hydrogen-bonding interaction (N^+–H···O) between **9c**,**d** and **10** is probably weakened to destabilize pseudorotaxane **9c-d·10**. Cu-crown ether interaction most likely disturbed the

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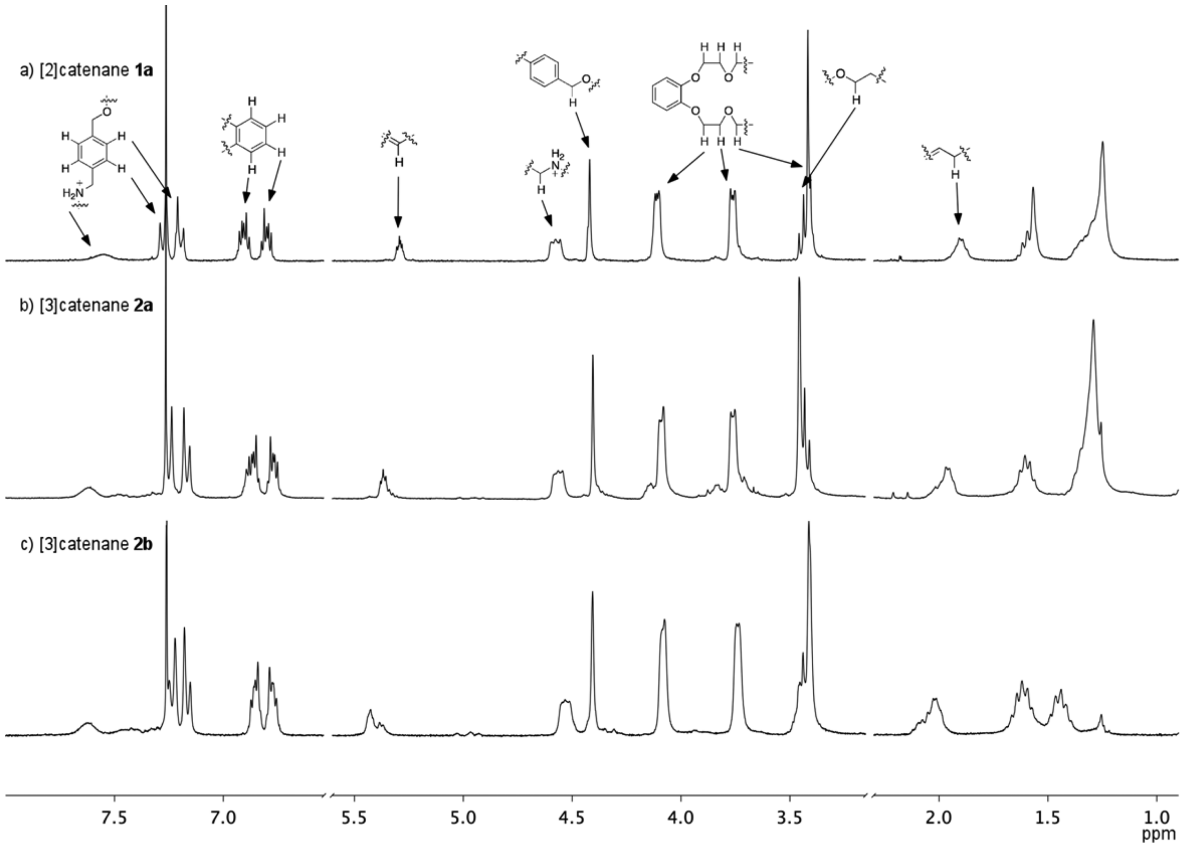

Figure 5. Partial ^{1}H NMR spectra (300 MHz) in $CDCl_3$ of (a) [2]catenane **1a**, (b) [3]catenane **2a**, and (c) [3]catenane **2b**.

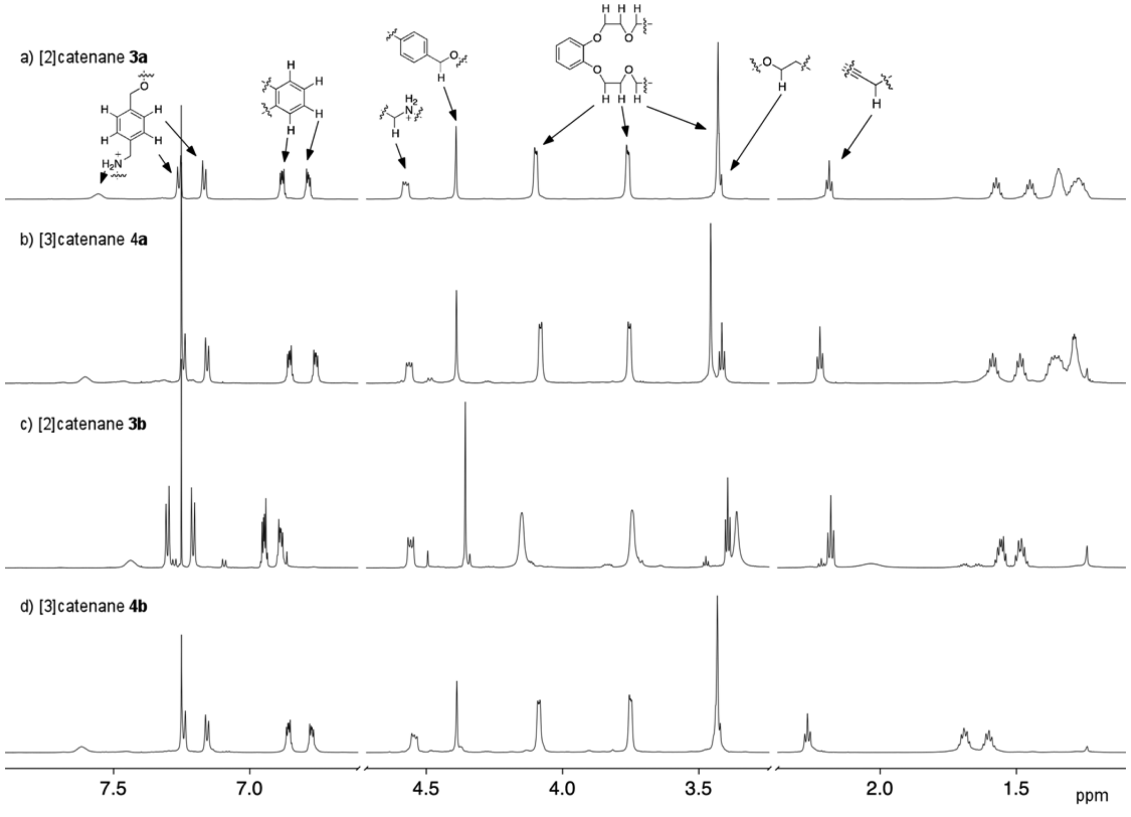

Figure 6. Partial ^{1}H NMR spectra (700 MHz) in $CDCl_3$ of (a) [2]catenane **3a**, (b) [3]catenane **4a**, (c) [2]catenane **3b**, and (d) [3]catenane **4b**.

complexation between ammonium salt and crown ether as well. The dethreading process competes with intra- and intermolecular oxidative acetylide coupling, resulting in a decrease in the formation of catenation products.

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Table 2. Yields of [2]Catenanes 1a,b and [3]Catenanes 2a,b and the Ratio of the Chemical Yields of [2]Catenane to [3]Catenane

ammonium salt	conc[a] (M)	yield (%) [2]catenane (%)	yield (%) [3]catenane (%)	ratio of chemical yields
9a	0.002	56	2	28
	0.01	41	16	2.6
	0.02	31	20	1.6
9b	0.002	0	25	0
	0.01	0	33	0
	0.02	0	35	0

[a]Both DB24C **10** and ammonium salt **9a** and **9b** were prepared in the same concentration.

Table 3. Yields of [2]Catenanes 3a,b and [3]Catenanes 4a,b and the Ratio of the Chemical Yields of [2]Catenane to [3]Catenane

ammonium salt	conc[a] (M)	yield (%) [2] catenane	yield (%) [3] catenane	Ratio of chemical yields
9c	0.002	23	4	5.8
	0.01	21	12	1.8
	0.02	12	8	1.5
9d	0.002	4	6	0.67
	0.01	6	15	0.40
	0.02	5	13	0.38

[a]Dibenzo[24]crown-8 (DB24C) **10** and ammonium salt **9c** and **9d** were prepared at the same concentration.

The correlation of the pseudorotaxane **9c,d·10** concentrations with the ratios of [2]catenane to [3]catenane was evaluated. As the concentration of **9c·10** increased from 0.002 to 0.02 M, the ratio decreased from 5.8 to 1.5. This trend was similar to that of olefin metathesis. Intramolecular processes involving pseudorotaxane **9c,d·10** are preferred over intermolecular processes in the concentration range of 0.002 to 0.02 M. Compound **9d** yielded [3]catenane **4b** as the major product[25] with ratios of 0.67, 0.40, and 0.38 when the concentrations of the substrates were 0.002, 0.01, and 0.02, respectively. As **9d·10** was concentrated, the ratio decreased, indicating a concentration dependence that was similar to that observed in other experiments. In the concentration range used in this study, the ratio was less than 1.0, indicating that the intramolecular process was preferred over the intramolecular process due to the short length of the ammonium salt.

Computational Studies of [2]Catenanes. Catenane formation results from the competition between intra- and intermolecular reactions. The intramolecular cyclization of pseudorotaxane **9a−d·10** that yields [2]catenanes **1a,b** and **3a,b** competes with the intermolecular reactions resulting in [3]catenane formation, [*n*]catenane formation, and intermolecular oligo- and polymerization. Although the catenane formation process is too complicated to be understood in detail, the rate of [2]catenane formation may be explained in terms of activation energies and the probability of end-to-end encounters.[26]

Activation energies are thought to reflect the strain energy for the formation of small and medium rings, while the ring strain of large-membered cyclic systems is commonly negligible.[27] In the formation process of [2]catenane, the crown ether should play an important role in steric repulsive forces. Therefore, the strain energies of [2]catenanes **1a,b** and **3a,b** may be informative. End-to-end encounters, which are associated with the entropic contribution of the reaction, likely decrease as the distance between the two reactive ends increases. Therefore, an increase in the length of the ammonium salts reduces the probability of the encounter between the two terminal olefins or acetylenes required for formation of [2]catenanes. The probabilities are also influenced by the flexibility of pseudorotaxanes **9a−d·10**. An increase in the length of the ammonium salts increases the flexibility of the pseudorotaxane, resulting in an increased entropic cost for the formation of [2]catenanes.

To estimate the steric interaction during the cyclization of pseudorotaxanes **9a−d·10**, molecular mechanics calculations of

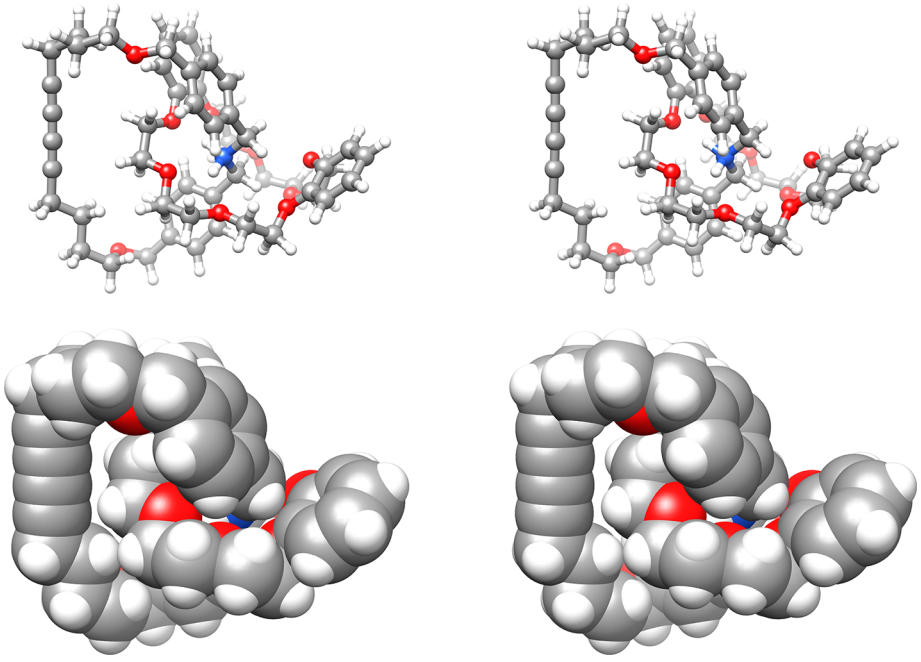

Figure 7. Stereoplots of the calculated structure of [2]catenane **3b**: ball and stick model (upper) and space-filling model (lower).

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the [2]catenanes were performed using MacroModel V9.1.[28] The initial geometries were generated using the Monte Carlo/low-mode search mixed method, and the structural optimizations were performed using the OPLS2005 force field with the GB/SA solvation parameters for chloroform.[29] A characteristic example of the calculated structures of [2]catenane **3b** is shown in Figure 7. The ammonium salt forms hydrogen-bonding interactions with the crown ethers and acquires a U-shaped conformation to wrap around one of the aromatic rings of the ammonium macrocycle. The cavities in the crown ether and the ammonium macrocycle are filled by each other, which suggests that the size of the ammonium macrocycle should be minimal for the formation of [2]catenane.

It is well-known that the ring strain of cyclized products is closely associated with the ease of cyclization of the chain molecules.[30] Therefore, the strain of the catenanes might govern the ease of cyclization. The ring strain energies of the catenanes can be estimated from the energy differences (ΔH) obtained from the energies of the catenanes and their components, which include cyclized ammonium macrocycles and crown ether **10**. The energies were calculated using density functional theory (DFT) calculations as implemented in Gaussian 09.[31] The initial geometries determined by the molecular mechanics method mentioned above were subjected to geometry optimization with B3LYP using the cc-pVTZ basis set (Table 4). The calculated

Table 4. Calculated Steric Energy, ΔH^a (kJ/mol), of Catenanes 1a,b and 3a,b

catenane	ΔH
1a	−154.06
1b	−150.30
3a	−143.64
3b	−144.89

[a]The calculated values were obtained using the following equation: $\Delta H = H_{\text{catenane}} - (H_{\text{macrocyclic ammonium salt}} + H_{\text{crown ether}})$.

ΔH values were large negative values, suggesting that all of the cyclization processes are enthalpically favorable. Compound **1a** experienced the largest increase (−154.06 kJ/mol) in ΔH, suggesting an ease of cyclization for [2]catenanes. This result is consistent with the fact that the ratio of the chemical yields of [2]catenane **1a** and [3]catenane **2a** is higher than those of the other catenanes. The enthalpic favorability should overcome the entropic disadvantage caused by the long length of the ammonium salt to afford [2]catenane **1a** in good yield. ΔH for **1b** was estimated to be −150.30 kJ/mol, which is larger than that of **1a**, which decreases the enthalpic advantage for the formation of **1b**. For oxidative acetylide coupling, **3a**, which contains a large ammonium macrocycle, has a calculated ΔH of −143.64 kJ/mol, which indicates an enthalpic preference for the formation of [2]catenanes, rather than entropic difficulty. Compound **3b**, which has an estimated ΔH of −144.89 kJ/mol, was more stable than **3a**. In addition to an entropic advantage, this enthalpic advantage most likely plays an important role in the formation of [2]catenane **3b**.

CONCLUSION

We have demonstrated the synthesis of [2]- and [3]catenanes under olefin metathesis and oxidative acetylide coupling conditions. Long ammonium salts containing two terminal reactive end-groups yielded [2]catenanes as the major products, while short ammonium salts afforded [3]catenanes as the major products. The concentrations of the starting substrates influenced the ratio of [2]catenane to [3]catenane. An increase in the concentration resulted in a decrease in the ratio. Molecular mechanics calculations and density functional theory explained the selective formation of [2]catenanes in terms of the steric factors affecting macrocyclization. This calculation method does not perfectly rationalize the selectivity of [2]- and [3]catenane formation but does provides some insight into estimating the selectivity.

EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C NMR spectra at high field were measured on a 700 MHz spectrometer (^{1}H: 700 MHz, ^{13}C: 175 MHz), a 400 MHz spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz), and a 300 MHz spectrometer (^{1}H: 300 MHz, ^{13}C: 75 MHz). ^{1}H NMR chemical shifts (δ) are given in ppm using tetramethylsilane as the internal standard. ^{13}C NMR chemical shifts (δ) are given in ppm from internal chloroform-*d* (δ = 77.0). The melting points were obtained on a micro melting apparatus and are uncorrected. The IR spectra were measured on an FT/IR spectrophotometer. The mass spectra were recorded with a high-resolution double-focusing mass spectrometer.

All of the reactions were performed under an argon atmosphere unless otherwise noted. Tetrahydrofuran (THF) was purchased as an anhydrous solvent and used directly. Dichloromethane was freshly distilled over P_2O_5. Column chromatography was performed using silica gel (particle size 100−210 μm). All reagents were of commercial grade and were used without further purification.

*Synthesis of N-(tert-Butoxycarbonyl)bis[4-[(dec-9-en-1-yloxy)-methyl]benzyl]amine (**7a**).* To a solution of NaH (55% dispersion in oil, 960 mg, 22.0 mmol) prewashed with hexane in DMF (20 mL) was added *N*-(*tert*-butoxycarbonyl)bis[4-(hydroxymethyl)benzyl]amine **5** (1.72 g, 4.79 mmol) in DMF (10 mL) at 0 °C. Then, a solution of dec-9-en-1-yl toluene-4-sulfonate (**6a**) (4.37 g, 14.1 mmol) in DMF (15 mL) was added to the reaction mixture. After being stirred for 24 h at 50 °C, the reaction mixture was poured into aqueous NH_4Cl. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and brine and then dried over anhydrous Na_2SO_4. After the Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by column chromatography on silica gel with 20% ethyl acetate in hexane to yield *N*-(*tert*-butoxycarbonyl)bis[4-[(dec-9-en-1-yloxy)methyl]benzyl]-amine (**7a**) (2.65 g, 4.19 mmol, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (d, J = 8.1 Hz, 4H), 7.19 (br, 4H), 5.81 (ddt, J = 17.1, 10.2, 6.6 Hz, 2H), 4.99 (ddt, J = 17.1, 2.1, 1.5 Hz, 2H), 4.93 (ddt, J = 10.2, 2.1, 1.2 Hz, 2H), 4.49 (s, 4H), 4.39 (br s, 2H), 4.31 (br s, 2H), 3.47 (t, J = 6.6 Hz, 4H), 2.04 (m, 4H), 1.62 (tt, J = 7.2, 6.6 Hz, 4H), 1.49 (s, 9H), 1.43−1.26 ppm (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156,0, 139.2, 137.7, 137.2, 128.0, 127.9, 127.4, 114.1, 80.0, 72.6, 70.6, 48.9, 48.6, 33.8, 29.8, 29.4, 29.1, 28.9, 28.4, 26.2 ppm. IR (neat): $1/\lambda$ = 3074, 2975, 2927, 2854, 1698, 1640, 1513, 1456, 1408, 1365, 1241, 1164, 1101, 1020 cm^{-1}. ESI-HRMS: m/z calcd for $C_{41}H_{63}NO_4$ [M + Na]$^+$ 656.4655, found 656.4673.

*Synthesis of Bis[4-[(dec-9-en-1-yloxy)methyl]benzyl]amine (**8a**).* To a solution of *N*-(*tert*-butoxycarbonyl)bis[4-[(dec-9-en-1-yloxy)-methyl]benzyl]amine (**7a**) (487 mg, 0.77 mmol) in CH_2Cl_2 (10 mL) was added trifluoroacetic acid (2.0 mL, 26.1 mmol) dropwise at 0 °C. After being stirred for 12 h at room temperature, the reaction mixture was poured into an aqueous 10% solution of NaOH. The aqueous layer was extracted with $CHCl_3$. After removal of the solvent in vacuo, the crude product was purified by column chromatography on silica gel with 20% ethyl acetate in hexane to yield bis[4-[(dec-9-en-1-yloxy)methyl]-benzyl]amine (**8a**) (353 mg, 0.66 mmol, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (m, 8H), 5.81 (ddt, J = 17.1, 10.2, 6.6 Hz, 2H), 4.99 (ddt, J = 17.1, 2.1, 1.5 Hz, 2H), 4.92 (ddt, J = 10.2, 2.1, 1.2 Hz, 2H), 4.48 (s, 4H), 3.79 (s, 4H), 3.45 (t, J = 6.6 Hz, 4H), 2.04 (m, 4H), 1.63−1.56 (m, 4H), 1.36−1.23 ppm (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.5, 139.2, 137.4, 128.1, 127.8, 114.1, 72.6, 70.5, 52.8, 33.8, 29.7, 29.4, 29.1, 28.9, 26.2 ppm. IR (neat): $1/\lambda$ = 3075, 2926, 2854, 1640, 1513,

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1458, 1359, 1099, 1020, 993, 909, 810 cm^{-1}. ESI-HRMS: m/z calcd for $C_{36}H_{55}NO_2$ $[M + H]^+$ 534.4311, found 534.4304.

*Synthesis of Bis[4-[(dec-9-en-1-yloxy)methyl]benzyl]ammonium Hexafluorophosphate (**9a**).* To a solution of bis[4-[(dec-9-en-1-yloxy)methyl]benzyl]amine (**8a**) (114 mg, 0.21 mmol) in acetone (5 mL), 6 M HCl was added dropwise at room temperature. After being stirred for 2 h, evaporation of the solvents produced a white solid that was dissolved in acetone (5 mL) and H_2O (20 mL). Excess NH_4PF_6 was added to the solution. After being stirred for 10 h, the reaction mixture was concentrated in vacuo. The aqueous layer was extracted with $CHCl_3$ and dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by precipitation with hexane from $CHCl_3$ to yield bis[4-[(dec-9-en-1-yloxy)methyl]benzyl]ammonium hexafluorophosphate (**9a**) (131 mg, 0.19 mmol, 92%) as a white solid. Mp: 81−83 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, J = 8.4 Hz, 4H), 7.33 (d, J = 8.4 Hz, 4H), 5.81 (ddt, J = 17.1, 10.2, 6.6 Hz, 2H), 4.98 (ddt, J = 17.1, 2.1, 1.5 Hz, 2H), 4.92 (ddt, J = 10.2, 2.1, 1.5 Hz, 2H), 4.46 (s, 4H), 4.11 (s, 4H), 3.47 (t, J = 6.6 Hz, 4H), 2.03 (m, 4H), 1.61 (m, 4H), 1.37−1.25 ppm (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2, 139.2, 129.9, 128.5, 127.9, 114.1, 72.0, 71.0, 50.8, 33.8, 29.7, 29.7, 29.4, 29.1, 28.9, 26.1. IR (KBr): $1/\lambda$ = 3246, 3225, 2923, 2852, 2793, 1642, 1467, 1417, 1362, 1104, 838 cm^{-1}. ESI-HRMS: m/z calcd for $C_{36}H_{56}F_6NO_2P$ $[M - PF_6]^+$ 534.4311, found 534.4307.

*Synthesis of N-(tert-Butoxycarbonyl)bis[4-[(hex-5-en-1-yloxy)-methyl]benzyl]amine (**7b**).* To a solution of NaH (60% dispersion in oil, 507 mg, 12.7 mmol) prewashed with hexane in DMF (20 mL) was added *N*-(*tert*-butoxycarbonyl)bis[4-(hydroxymethyl)benzyl]amine **5** (1.20 g, 3.36 mmol) in DMF (10 mL) at room temperature. Then, a solution of hex-5-en-1-yl toluene-4-sulfonate (**6b**) (1.90 g, 7.47 mmol) in DMF (10 mL) was added to the reaction mixture. After being stirred for 12 h under reflux conditions, the reaction mixture was poured into aqueous NH_4Cl. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and brine and then dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by column chromatography on silica gel with 20% ethyl acetate in hexane to yield *N*-(*tert*-butoxycarbonyl)bis[4-[(hex-5-en-1-yloxy)-methyl]benzyl]amine (**7b**) (695 mg, 1.33 mmol, 40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31 (d, J = 8.1 Hz, 4H), 7.19 (br, 4H), 5.82 (ddt, J = 17.1, 10.2, 6.6 Hz, 2H), 5.05 (ddt, J = 17.1, 1.8, 1.5 Hz, 2H), 4.95 (ddt, J = 10.2, 1.8, 1.5 Hz, 2H), 4.49 (s, 4H), 4.40 (br s, 2H), 3.31 (br s, 2H), 3.49 (t, J = 6.6 Hz, 4H), 2.08 (ddq, J = 6.6, 6.6, 1.5 Hz, 4H), 1.70−1.60 (m, 4H), 1.49 (s, 9H), 1.43−1.26 ppm (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 138.7, 137.6, 137.2, 128.0, 127.8, 127.4, 114.5, 80.0, 72.6, 70.2, 48.8, 48.5, 33.5, 29.2, 28.4, 25.4 ppm. IR (neat): $1/\lambda$ = 3074, 2975, 2933, 2857, 1695, 1640, 1513, 1455 cm^{-1}. ESI-HRMS: m/z calcd for $C_{33}H_{47}NO_4$ $[M + Na]^+$ 544.3403, found 544.3416.

*Synthesis of Bis[4-[(hex-5-en-1-yloxy)methyl]benzyl]amine (**8b**).* To a solution of *N*-(*tert*-butoxycarbonyl)bis[4-[(dec-9-en-1-yloxy)-methyl]benzyl]amine (**7b**) (981 mg, 1.88 mmol) in CH_2Cl_2 (20 mL) was added trifluoroacetic acid (3.0 mL, 39.2 mmol) dropwise at 0 °C. After being stirred for 12 h at room temperature, the reaction mixture was poured into an aqueous 10% solution of NaOH. The aqueous layer was extracted with $CHCl_3$. After removal of the solvent in vacuo, the crude product was purified by column chromatography on silica gel with 20% ethyl acetate in hexane to yield bis[4-[(hex-5-en-1-yloxy)methyl]-benzyl]amine (**8b**) (691 mg, 1.64 mmol, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (m, 8H), 5.97 (ddt, J = 17.1, 10.5, 5.4 Hz, 2H), 5.22 (ddt, J = 17.1, 1.8, 1.5 Hz, 2H), 4.99 (ddt, J = 10.5, 1.8, 1.5 Hz, 2H), 4.50 (s, 4H), 3.80 (s, 4H), 3.48 (tt, J = 6.3, 1.2 Hz, 4H), 2.08 (m, 4H), 1.65 (m, 4H), 1.50 ppm (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.5, 138.7, 137.3, 128.1, 127.7, 114.4, 72.6, 70.1, 52.7, 33.5, 29.2, 25.4 ppm. IR (neat): $1/\lambda$ = 3073, 2934, 2856, 1639, 1455, 1359, 1100, 994, 910, 811 cm^{-1}. ESI-HRMS m/z calcd for $C_{28}H_{39}NO_2$ $[M + H]^+$ 422.3059, found 422.3063.

*Synthesis of Bis[4-[(hex-5-en-1-yloxy)methyl]benzyl]ammonium Hexafluorophosphate (**9b**).* To a solution of bis[4-[(hex-5-en-1-yloxy)methyl]benzyl]amine (**8b**) (691 mg, 1.63 mmol) in acetone (10 mL), 6 M HCl was added dropwise at room temperature. After being stirred for 2 h, evaporation of the solvents produced a white solid that was dissolved in acetone (10 mL) and H_2O (40 mL). Excess NH_4PF_6 was added to the solution. After being stirred for 10 h, the reaction mixture was concentrated in vacuo. The aqueous layer was extracted with $CHCl_3$ and dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by precipitation with hexane from $CHCl_3$ to yield bis[4-[(hex-5-en-1-yloxy)methyl]benzyl]ammonium hexafluorophosphate (**9b**) (878 mg, 1.54 mmol, 94%). Mp: 77 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40 (d, J = 8.1 Hz, 4H), 7.33 (d, J = 8.1 Hz, 4H), 6.74 (br s, 2H), 5.80 (ddt, J = 17.1, 10.2, 6.6 Hz, 2H), 5.00 (ddt, J = 17.1, 2.1, 1.5 Hz, 2H), 4.94 (ddt, J = 10.2, 2.1, 1.5 Hz, 2H), 4.46 (s, 4H), 4.13 (t, J = 5.1 Hz, 4H), 3.47 (t, J = 6.6 Hz, 4H), 2.07 (m, 4H), 1.64 (m, 4H), 1.47 ppm (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6, 130.0, 128.5, 114.6, 72.0, 70.7, 50.8, 33.5, 29.1, 25.4 ppm. IR (KBr): $1/\lambda$ = 3289, 2931, 2854, 2115, 1414, 1106, 842 cm^{-1}. ESI-HRMS: m/z calcd for $C_{28}H_{40}F_6NO_2P$ $[M - PF_6]^+$ 422.3059, found 422.3080.

*Synthesis of N-(tert-Butoxycarbonyl)bis[4-[(dec-9-yn-1-yloxy)-methyl]benzyl]amine (**7c**).* To a solution of NaH (60% dispersion in oil, 2.08 g, 52.0 mmol) prewashed with hexane in DMF (30 mL) was added *N*-(*tert*-butoxycarbonyl)bis[4-(hydroxymethyl)benzyl]amine **5** (3.67 g, 10.3 mmol) in DMF (30 mL) at 0 °C under N_2. Then, a solution of dec-9-yn-1-yl toluene-4-sulfonate (**6c**) (7.92 g, 25.7 mmol) in DMF (30 mL) and catalytic amounts of tetrabutylammonium iodide were added to the reaction mixture. After being stirred for 15 h at 50 °C, the reaction mixture was poured into aqueous NH_4Cl. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and brine and then dried over anhydrous Na_2SO_4. After Na_2SO_4 was remvoed by filtration, the solvent was concentrated in vacuo. The crude product was purified by column chromatography on silica gel with 10% ethyl acetate in hexane to yield *N*-(*tert*-butoxycarbonyl)bis[4-[(dec-9-yn-1-yloxy)methyl]benzyl]amine (**7c**) (5.38 g, 8.54 mmol, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, J = 8.1 Hz, 4H), 7.16 (br, 4H), 4.47 (s, 4H), 4.37 (br, 2H), 4.28 (br, 2H), 3.45 (t, J = 6.6 Hz, 4H), 2.16 (dt, J = 7.1, 2.6 Hz, 4H), 1.91 (t, J = 2.6 Hz, 2H), 1.66−1.44 (m, 17H), 1.42−1.24 ppm (m, 16H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 137.7, 137.2, 128.0, 127.8, 127.4, 84.7, 80.0, 72.6, 70.5, 68.1, 48.9, 48.5, 29.7, 29.3, 29.0, 28.7, 28.4, 26.1, 18.4 ppm. IR (neat): $1/\lambda$ = 3306, 2932, 2856, 2117, 1694, 1242, 1100, 883 cm^{-1}. ESI-HRMS: m/z calcd for $C_{41}H_{59}NO_4$ $[M + Na]^+$ 652.4336, found 652.4333. Anal. Calcd for $C_{41}H_{59}NO_4 \cdot {}^1/_2H_2O$: C, 77.07; H, 9.47; N, 2.19. Found: C, 77.25; H, 9.35; N, 2.15.

*Synthesis of Bis[4-[(dec-9-yn-1-yloxy)methyl]benzyl]amine (**8c**).* To a solution of *N*-(*tert*-butoxycarbonyl)bis[4-[(dec-9-yn-1-yloxy)-methyl]benzyl]amine (**7c**) (4.95 g, 7.86 mmol) in CH_2Cl_2 was added trifluoroacetic acid (5.2 mL, 67.9 mmol) dropwise at 0 °C under N_2. After being stirred for 4 h at room temperature, the reaction mixture was poured into aqueous $NaHCO_3$ and basified with $NaHCO_3$ powder. The aqueous layer was extracted with $CHCl_3$. The organic layer was washed with saturated $NaHCO_3$ and brine and then dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by column chromatography on silica gel with 40% ethyl acetate in hexane to yield bis[4-[(dec-9-yn-1-yloxy)methyl]benzyl]amine (**8c**) (4.00 g, 7.55 mmol, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34−7.29 (m, 8H), 4.48 (s, 4H), 3.79 (s, 4H), 3.45 (t, J = 6.6 Hz, 4H), 2.17 (dt, J = 7.1, 2.7 Hz, 4H), 1.93 (t, J = 2.7 Hz, 2H), 1.62−1.50 (m, 8H), 1.39−1.28 ppm (m, 16H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.4, 137.4, 128.2, 127.7, 84.7, 72.6, 70.4, 68.1, 52.7, 29.7, 29.3, 29.0, 28.7, 28.4, 26.1, 18.4 ppm. IR (neat): $1/\lambda$ = 3294, 2933, 2116, 1703, 1513, 1462, 1097, 814 cm^{-1}. ESI-HRMS: m/z calcd for $C_{36}H_{51}NO_2$ $[M + H]^+$ 530.3993, found 530.3977. Anal. Calcd for $C_{36}H_{51}NO_2 \cdot H_2O$: C, 78.93; H, 9.75; N, 2.56. Found: C, 78.92; H, 9.44; N, 2.53.

*Synthesis of Bis[4-[(dec-9-yn-1-yloxy)methyl]benzyl]ammonium Hexafluorophosphate (**9c**).* To a solution of bis[4-[(dec-9-yn-1-yloxy)methyl]benzyl]amine (**8c**) (4.00 g, 7.55 mmol) in acetone (50 mL) was added 6 M HCl (2.6 mL) dropwise at room temperature. After being stirred for 2 h, the reaction mixture was concentrated in vacuo. Then, acetone (70 mL) and a solution of NH_4PF_6 (3.04 g, 18.65 mmol) in water were added to the compound. After being stirred for 4 h, the

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reaction mixture was concentrated in vacuo. The aqueous layer was extracted with $CHCl_3$ and dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by precipitation with hexane from $CHCl_3$ to yield bis[4-[(dec-9-yn-1-yloxy)methyl]benzyl]ammonium hexafluorophosphate (**9c**) (4.54 g, 6.71 mmol, 89%). Mp: 103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40−7.24 (m, 8H), 4.46 (s, 4H), 4.10 (s, 4H), 3.46 (t, J = 6.5 Hz, 4H), 2.16 (dt, J = 7.1, 2.6 Hz, 4H), 1.92 (t, J = 2.6 Hz, 2H), 1.54−1.47 (m, 8H), 1.39−1.28 ppm (m, 16H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.1, 129.9, 128.5, 128.0, 84.8, 72.0, 71.0, 68.1, 50.7, 29.7, 29.3, 29.0, 28.7, 28.4, 26.1, 18.4 ppm. IR (KBr): $1/\lambda$ = 3289, 2931, 2854, 2115, 1414, 1106, 842 cm^{-1}. ESI-HRMS: m/z calcd for $C_{36}H_{52}F_6NO_2P$ $[M - PF_6]^+$ 530.3993, found 530.3980.

*Synthesis of N-(tert-Butoxycarbonyl)bis[4-[(hex-5-yn-1-yloxy)-methyl]benzyl]amine (**7d**).* To a solution of NaH (60% dispersion in oil, 3.37 g, 84.3 mmol) prewashed with hexane in DMF (80 mL) was added *N*-(*tert*-butoxycarbonyl)bis[4-(hydroxymethyl)benzyl]amine **5** (5.92 g, 16.6 mmol) in DMF (40 mL) at 0 °C under N_2. Then, a solution of hex-5-yn-1-yl toluene-4-sulfonate (**6d**) (9.61 g, 38.1 mmol) in DMF (40 mL) and catalytic amounts of tetrabutylammonium iodide were added to the reaction mixture. After being stirred for 2 h at 50 °C, the reaction mixture was poured into aqueous NH_4Cl. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and brine and then dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by column chromatography on silica gel with 10% ethyl acetate in hexane to yield *N*-(*tert*-butoxycarbonyl)bis[4-[(hex-5-yn-1-yloxy)methyl]benzyl]amine (**7d**) (7.41 g, 14.3 mmol, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (d, J = 8.4 Hz, 4H), 7.20 (br, 4H), 4.49 (s, 4H), 4.39 (br, 2H), 4.30 (br, 2H), 3.50 (t, J = 6.2 Hz, 4H), 2.22 (dt, J = 7.0, 2.6 Hz, 4H), 1.95 (t, J = 2.6 Hz, 2H), 1.80−1.59 (m, 8H), 1.49 ppm (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 137.5, 137.3, 128.1, 127.9, 127.5, 84.3, 80.1, 72.6, 69.8, 68.4, 48.9, 48.5, 28.8, 28.5, 25.2, 18.2 ppm. IR (neat): $1/\lambda$ = 3295, 2936, 2863, 2116, 1693, 1243, 1113, 883 cm^{-1}. ESI-HRMS: m/z calcd for $C_{33}H_{43}NO_4$ $[M + Na]^+$ 540.3084, found 540.3082. Anal. Calcd for $C_{33}H_{43}NO_4 \cdot {}^1/_4H_2O$: C, 75.90; H, 8.40; N, 2.68. Found: C, 76.08; H, 8.43; N, 2.65.

*Synthesis of Bis[4-[(hex-5-yn-1-yloxy)methyl]benzyl]amine (**8d**).* To a solution of *N*-(*tert*-butoxycarbonyl)bis[4-[(hex-5-yn-1-yloxy)-methyl]benzyl]amine (**7d**) (4.61 g, 8.90 mmol) in CH_2Cl_2 was added trifluoroacetic acid (6.8 mL, 88.8 mmol) dropwise at 0 °C under N_2. After being stirred for 3 h at room temperature, the reaction mixture was poured into aqueous $NaHCO_3$ and basified with $NaHCO_3$ powder. The aqueous layer was extracted with $CHCl_3$. The organic layer was washed with saturated $NaHCO_3$ and brine and then dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The crude product was purified by column chromatography on silica gel with 40% ethyl acetate in hexane to yield bis[4-[(hex-5-yn-1-yloxy)methyl]benzyl]amine (**8d**) (3.66 g, 8.76 mmol, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32−7.27 (m, 8H), 4.47 (s, 4H), 3.77 (s, 4H), 3.47 (t, J = 6.2 Hz, 4H), 2.20 (dt, J = 7.0, 2.6 Hz, 4H), 1.93 (t, J = 2.6 Hz, 2H), 1.79−1.53 ppm (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.3, 137.3, 128.2, 127.8, 84.3, 72.7, 69.7, 68.4, 52.7, 28.7, 25.2, 18.2 ppm. IR (neat): $1/\lambda$ = 3305, 2941, 2115, 1643, 1514, 1454, 1093, 808 cm^{-1}. ESI-HRMS: m/z calcd for $C_{28}H_{35}NO_2$ $[M + H]^+$ 418.2741, found 418.2729. Anal. Calcd for for $C_{28}H_{35}NO_2 \cdot {}^1/_2H_2O$: C, 78.83; H, 8.51; N, 3.28. Found: C, 78.81; H, 8.33; N, 3.20.

*Synthesis of Bis[4-[(hex-5-yn-1-yloxy)methyl]benzyl]ammonium Hexafluorophosphate (**9d**).* To a solution of bis[4-[(hex-5-yn-1-yloxy)methyl]benzyl]amine (**8d**) (3.66 g, 8.76 mmol) in acetone (55 mL) was added 6 M HCl (3 mL) dropwise at room temperature. After being stirred for 2 h, the reaction mixture was concentrated in vacuo. Then, acetone (50 mL) and a solution of NH_4PF_6 (2.86 g, 17.55 mmol) in water were added to the compound. After being stirred for 4 h, the reaction mixture was concentrated in vacuo. The aqueous layer was extracted with $CHCl_3$ and then dried over anhydrous Na_2SO_4. After removing the Na_2SO_4 by filtration, the solvent was concentrated in vacuo. The crude product was purified by precipitation with hexane from $CHCl_3$ to yield bis[4-[(hex-5-yn-1-yloxy)methyl]benzyl]-ammonium hexafluorophosphate (**9d**) (4.24 g, 7.52 mmol, 86%). Mp: 111 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42−7.34 (m, 8H), 4.48 (s, 4H), 4.12 (s, 4H), 3.51 (t, J = 6.3 Hz, 4H), 2.22 (dt, J = 7.0, 2.6 Hz, 4H), 1.95 (t, J = 2.6 Hz, 2H), 1.78−1.71 (m, 4H), 1.65−1.59 ppm (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.5, 130.0, 128.6, 128.4, 84.2, 72.1, 70.2, 68.6, 50.3, 28.6, 25.1, 18.2 ppm. IR (neat): $1/\lambda$ = 3286, 2943, 2863, 2114, 1416, 1104, 837 cm^{-1}. ESI-HRMS: m/z calcd for $C_{28}H_{36}F_6NO_2P$ $[M - PF_6]^+$ 418.2741, found 418.2731.

General Procedure of Catenane Synthesis Using Olefin Metathesis. To a solution of ammonium hexafluorophosphate salts **9a**,**b** containing a terminal olefin (1 equiv) and dibenzo[24]crown-8 (DB24C) (**10**) (1 equiv) in CH_2Cl_2 was added first-generation Grubbs catalyst (0.2 equiv) at room temperature under Ar. The concentrations were varied from 0.002 to 0.02 M. After being stirred for 0.5 days under reflux conditions, the reaction mixture was passed through a silica gel column with 10% methanol in chloroform. The crude product was purified by GPC with chloroform to yield [2]catenane **1** and [3]catenane **2**.

*Synthesis of [2]Catenane **1a** and [3]Catenane **2a**.* Following the above general procedure, bis[4-[(dec-9-en-1-yloxy)methyl]benzyl]-ammonium hexafluorophosphate (**9a**) (70 mg, 0.10 mmol), dibenzo[24]-crown-8 (DB24C) (**10**) (45 mg, 0.10 mmol), and Grubbs catalyst first (17 mg, 0.021 mmol) in CH_2Cl_2 (5 mL for 0.02 M) yielded [2]catenane **1a** (35 mg, 0.032 mmol, 31%) and [3]catenane **2a** (23 mg, 0.010 mmol, 20%).

*[2]Catenane **1a**.* ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (br, 2H), 7.28 (d, J = 7.9 Hz, 4H), 7.20 (d, J = 7.9 Hz, 4H), 6.93−6.88 (m, 4H), 6.82−6.78 (m, 4H), 5.31−5.28 (m, 2H), 4.59−4.55 (m, 4H), 4.42(s, 4H), 4.12−4.10 (m, 8H), 3.77−3.75 (m, 8H), 3.46−3.41 (m, 12H), 1.93−1.87 (m, 4H), 1.64−1.57 (m, 8H), 1.37−1.25 ppm (m, 16H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.4, 140.2, 130.7, 130.3, 129.3, 127.8, 121.8, 112.8, 72.0, 70.6, 70.3, 70.1, 68.3, 52.3, 32.4, 29.7, 29.6, 29.5, 29.1, 28.7, 26.4 ppm. IR ($CHCl_3$): $1/\lambda$ = 3153, 2929, 1596, 1504, 1251, 1106, 848, 772 cm^{-1}. ESI-HRMS: m/z calcd for $C_{58}H_{84}F_6NO_{10}P$ $[M - PF_6]^+$ 954.6090, found 954.6084.

*[3]Catenane **2a**.* ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (br, 4H), 7.25 (d, J = 8.0 Hz, 8H), 7.17 (d, J = 8.0 Hz, 8H), 6.89−6.84 (m, 8H), 6.79−6.75 (m, 8H), 5.38−5.34 (m, 4H), 4.58−4.54 (m, 8H), 4.40 (s, 8H), 4.10−4.08 (m, 16H), 3.77−3.75 (m, 16H), 3.45−3.41 (m, 24H), 2.05−1.95 (m, 8H), 1.65−1.56 (m, 16H), 1.35−1.26 ppm (m, 32H). ^{13}C NMR (175 MHz, $CDCl_3$): δ = 147.4, 140.1, 130.6, 130.3, 129.1, 127.5, 121.6, 112.6, 72.0, 70.7, 70.6, 70.1, 68.1, 52.4, 32.5, 29.7, 29.4, 29.4, 29.3, 28.9, 26.1 ppm. IR ($CHCl_3$): $1/\lambda$ = 3150, 2929, 1596, 1504, 1251, 1104, 848, 771 cm^{-1}. ESI-HRMS m/z calcd for $C_{116}H_{168}F_{12}N_2O_{20}P_2$ $[M - 2PF_6]^{2+}$ 955.1107, found 955.1084.

*Synthesis of [3]Catenane **2b**.* Following the above general procedure, bis[4-[(hex-5-en-1-yloxy)methyl]benzyl]ammonium hexafluorophosphate (**9b**) (70 mg, 0.12 mmol), dibenzo[24]crown-8 (DB24C) (**10**) (55 mg, 0.12 mmol), and Grubbs catalyst first (17 mg, 0.0021 mmol) in CH_2Cl_2 (6 mL for 0.02 M) yielded [3]catenane **2b** (42 mg, 0.021 mmol, 35%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (br, 4H), 7.23 (d, J = 7.8 Hz, 8H), 7.17 (d, J = 7.8 Hz, 8H), 6.87−6.84 (m, 8H), 6.79−6.76 (m, 8H), 5.44−5.37 (m, 4H), 4.55−4.51 (m, 8H), 4.41 (s, 8H), 4.09−4.08 (m, 16H), 3.75−3.73 (m, 16H), 4.45−3.41 (m, 24H), 2.11−1.99 (m, 8H), 1.67−1.57 (m, 8H), 1.49−1.39 ppm (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$); δ = 147.4, 140.1, 130.5, 130.3, 129.1, 127.4, 121.6, 112.7, 71.9, 70.6, 70.5, 70.1, 68.2, 52.4, 32.3, 29.1, 26.2 ppm. IR ($CHCl_3$): $1/\lambda$ = 3148, 2932, 1596, 1504, 1249, 1108, 847, 776 cm^{-1}. ESI-HRMS m/z calcd for $C_{100}H_{136}F_{12}N_2O_{20}P_2$ $[M - 2PF_6]^{2+}$ 842.9855, found 842.9835.

General Procedure of Catenane Synthesis Using Eglinton Coupling. To a solution of ammonium hexafluorophosphate salts **9c**−**d** containing a terminal alkyne (1 equiv) and dibenzo[24]crown-8 (DB24C) (**10**) (1 equiv) in CH_2Cl_2 were added $Cu(OAc)_2$ (3 equiv) and pyridine (1 equiv) at room temperature under N_2. The concentrations were varied from 0.002 to 0.02 M. After being stirred for 2.5 days at reflux, the reaction mixture was filtered with Celite. The filtrate was washed with $NH_4Cl/NaHCO_3$ aqueous solution, 1 M NaOH, saturated $NaHCO_3$, and brine and dried over anhydrous Na_2SO_4. After Na_2SO_4 was removed by filtration, the solvent was concentrated in vacuo. The residue was dissolved in CH_2Cl_2 and treated

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with a solution of excess NH_4PF_6 in water at room temperature. After being stirred for 5 h, the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4. After removing the Na_2SO_4 by filtration, the solvent was concentrated in vacuo. The crude product was purified by column chromatography on silica gel with 10% methanol in $CHCl_3$ and GPC ($CHCl_3$) to yield [2]catenane **3a,b** and [3]catenane **4a,b**.

*Synthesis of [2]Catenane **3a** and [3]Catenane **4a**.* Following the above general procedure, bis[4-[(dec-9-yn-1-yloxy)methyl]benzyl]-ammonium hexafluorophosphate (**9c**) (135.3 mg, 0.200 mmol), dibenzo[24]crown-8 (DB24C) (**10**) (89.5 mg, 0.200 mmol), $Cu(OAc)_2$ (110.2 mg, 0.607 mmol), and pyridine (16.5 μL, 0.204 mmol) in CH_2Cl_2 (10 mL) yielded [2]catenane **3a** (28.1 mg, 0.025 mmol, 12%) and [3]catenane **4a** (18.0 mg, 0.008 mmol, 8%).

*[2]Catenane **3a**.* ^{1}H NMR (700 MHz, $CDCl_3$): δ = 7.56 (br, 1H), 7.26 (d, J = 8.0 Hz, 4H), 7.26 (d, J = 8.0 Hz, 4H), 6.88−6.87 (m, 4H), 6.79−6.78 (m, 4H), 4.58−4.57 (m, 4H), 4.39 (s, 4H), 4.10−4.09 (m, 8H), 3.77−3.75 (m, 8H), 3.43−3.42 (m, 12H), 2.19 (t, J = 6.7 Hz, 4H), 1.59−1.55 (m, 4H), 1.47−1.43 (m, 4H), 1.36−1.25 ppm (m, 16H). ^{13}C NMR (175 MHz, $CDCl_3$): δ = 147.4, 140.2, 130.7, 129.2, 127.6, 121.7, 112.8, 77.6, 72.0, 70.6, 70.3, 70.1, 68.2, 65.3, 52.3, 29.7, 29.1, 29.1, 28.4, 28.2, 26.3, 19.0 ppm. IR ($CHCl_3$): $1/\lambda$ = 3152, 2933, 1595, 1503, 1251, 1106, 850, 758 cm^{-1}. ESI-HRMS: m/z calcd for $C_{60}H_{82}F_6NO_{10}P$ [M − PF_6]$^+$ 976.5933, found 976.5910.

*[3]Catenane **4a**.* ^{1}H NMR (700 MHz, $CDCl_3$): δ = 7.60 (br, 2H), 7.25 (d, J = 7.6 Hz, 8H), 7.16 (d, J = 7.6 Hz, 8H), 6.86−6.85 (m, 8H), 6.77−6.75 (m, 8H), 4.57−4.55 (m, 8H), 4.39 (s, 8H), 4.09−4.03 (m, 16H), 3.76−3.75 (m, 16H), 3.46 (s, 16H), 3.42 (t, J = 6.5 Hz, 8H), 2.22 (t, J = 6.8 Hz, 8H), 1.61−1.57 (m, 8H), 1.51−1.47 (m, 8H), 1.39−1.24 ppm (m, 32H). ^{13}C NMR (175 MHz, $CDCl_3$): δ = 147.4, 140.1, 130.6, 129.1, 127.5, 121.6, 112.6, 77.5, 72.0, 70.7, 70.1, 68.1, 65.3, 52.4, 29.6, 29.2, 29.0, 28.6, 28.2, 26.1, 19.1 ppm. IR ($CHCl_3$): $1/\lambda$ = 3151, 2933, 1595, 1504, 1251, 1104, 848, 755 cm^{-1}. ESI-HRMS: m/z calcd for $C_{120}H_{164}F_{12}N_2O_{20}P_2$ [M − 2PF_6]$^{2+}$ 977.0950, found 977.0935.

*Synthesis of [2]Catenane **3b** and [3]Catenane **4b**.* Following the above general procedure, bis[4-[(hex-5-yn-1-yloxy)methyl]benzyl]-ammonium hexafluorophosphate (**9d**) (112.5 mg, 0.200 mmol), dibenzo[24]crown-8 (DB24C) (**10**) (89.2 mg, 0.199 mmol), $Cu(OAc)_2$ (110.2 mg, 0.607 mmol), and pyridine (16.5 μL, 0.204 mmol) in CH_2Cl_2 (10 mL) yielded [2]catenane **3b** (10.1 mg, 0.010 mmol, 5%), and [3]catenane **4b** (26.3 mg, 0.013 mmol, 13%).

*[2]Catenane **3b**.* ^{1}H NMR (700 MHz, $CDCl_3$): δ = 7.44 (br, 1H), 7.31 (d, J = 7.9 Hz, 4H), 7.21 (d, J = 7.9 Hz, 4H), 6.95−6.94 (m, 4H), 6.89−6.88 (m, 4H), 4.57−4.55 (m, 4H), 4.36 (s, 4H), 4.15 (s, 8H), 3.74 (s, 8H), 3.39 (t, J = 5.7 Hz, 4H), 3.36 (s, 8H), 2.18 (t, J = 7.4 Hz, 4H), 1.58−1.54 (m, 4H), 1.52−1.45 ppm (m, 4H). ^{13}C NMR (175 MHz, $CDCl_3$): δ = 147.7, 139.9, 131.2, 129.8, 129.1, 121.9, 113.2, 77.8, 72.4, 70.5, 70.1, 69.2, 68.6, 65.1, 52.3, 29.3, 26.3, 19.0 ppm. IR ($CHCl_3$): $1/\lambda$ = 3154, 2932, 1595, 1503, 1252, 1108, 848, 745 cm^{-1}. ESI-HRMS m/z calcd for $C_{52}H_{66}F_6NO_{10}P$ [M − PF_6]$^+$ 864.4681, found 864.4646.

*[3]Catenane **4b**.* ^{1}H NMR (700 MHz, $CDCl_3$): δ = 7.62 (br, 2H), 7.25 (d, J = 7.8 Hz, 8H), 7.16 (d, J = 7.8 Hz, 8H), 6.87−6.85 (m, 8H), 6.79−6.76 (m, 8H), 4.55−4.53 (m, 8H), 4.39 (s, 8H), 4.09−4.08 (m, 16H), 3.76−3.75 (m, 16H), 3.45−3.42 (m, 24H), 2.27 (t, J = 7.0 Hz, 8H), 1.71−1.58 ppm (m, 16H). ^{13}C NMR (175 MHz, $CDCl_3$): δ = 147.4, 139.9, 130.6, 129.1, 127.5, 121.6, 112.7, 77.3, 72.0, 70.6, 70.1, 69.8, 68.2, 65.5, 52.3, 28.7, 25.2, 18.9 ppm. IR ($CHCl_3$): $1/\lambda$ = 3150, 2934, 1595, 1504, 1252, 1107, 848, 751 cm^{-1}. ESI-HRMS: m/z calcd for $C_{104}H_{132}F_{12}N_2O_{20}P_2$ [M − 2PF_6]$^{2+}$ 864.9698, found 864.9670.

Determination of the Association Constants. The association constants for ammonium salts **9a−d** and crown ether **10** were determined by ^{1}H NMR titration in dichloromethane-d_2. The complexes of **9a−d** with **10** at 25 °C were in slow exchange on the NMR time scale and displayed well-resolved signals for the free and bound forms. The relative intensities of the protons of free and bound **9a−d**, along with the known concentrations of **9a−d** and **10**, were used to determine the association constants (K_a's) at 25 °C.

Molecular Modeling. Molecular mechanics calculations were performed on the catenanes with the MacroModel V9.1 program package. Five thousand initial geometries were generated by a low-mode and Monte Carlo mixed search option, and the given geometries were optimized by a conjugate gradient energy minimization using the OPLS2005 force field with the GB/SA solvation parameters for $CHCl_3$.

Density functional theory (DFT) calculations were performed as implemented in Gaussian 09. The initial geometries were determined by molecular mechanics method using the OPLS2005 force field in the MacroModel V9.1 program package. The geometries were subjected to geometry optimization using B3LYP and the cc-pVTZ basis set.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C spectra of new compounds; atomic coordinates of [2]catenane. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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