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Rapid and High-Yield Synthesis of [23]Crown Ether: Applied as a Wheel Component in the Formation of Pseudo[2]rotaxane and Synthesis of [2]Catenane with a Dibenzylammonium Dumbbell

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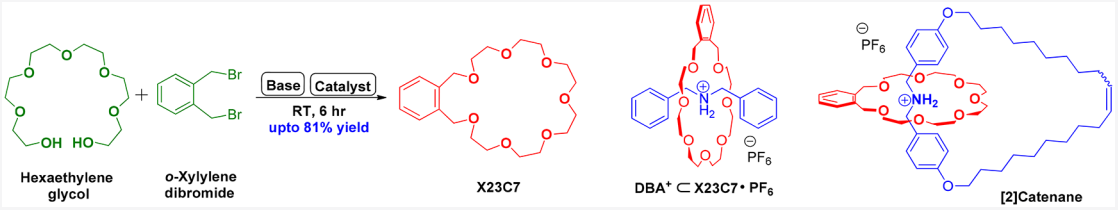

ABSTRACT: A facile, rapid, and high yield synthesis of [23]crown ether (X23C7) has been developed from commercially available starting materials, in one step with good to excellent yield. The reaction is completed in 6 h under room temperature conditions, with the highest yield being 81%. The X23C7 macrocycle formed pseudo[2]rotaxane with a dibenzylammonium ion (DBA^+) dumbbell, exhibiting strong association (K_a = 2.61 × 10^3 M^{-1}). Consequently, a [2]catenane was synthesized from a DBA^+-based diolefin terminated salt and X23C7 in 81% yield, using a threading-followed-ring-closing-metathesis approach.

Mechanically interlocked molecules (MIMs)[1] are of considerable interest in the scientific community due to their broad range of applications as molecular switch based molecular scale electronics,[2] molecular actuators,[3] molecular elevators,[4] smart surfaces,[5] and controlled drug release.[6] MIMs have also been incorporated in metal−organic frameworks (MOFs).[7] Catenane[8] and rotaxane[9] happen to be the simplest and fundamental class of MIMs, which are synthetically obtained from the noncovalent template-directed synthesis. Among the hydrogen bond templates,[10] DBA^+ (dibenzylammonium)-[24]crown ether (especially dibenzo-24-crown-8, DB24C8) is one of the most widely used and prominent complementary recognition pairs. DBA^+-DB24C8 has been extensively utilized to construct novel architectures,[11] responsive polymers,[12] responsive nanofibers,[13] fluorescent sensors,[14] light-harvesting antennas,[15] molecular elevators,[4] molecular information ratchets,[16] nanovalves,[17] and other stimuli-responsive molecular switches.[18] The DBA^+-DB24C8 recognition pair involves H-bonding ([N^+−H···O], [C−H···O]), and electrostatic ([N^+···O]) interactions. The recognition ability of DB24C8 is generally attributed to its [24]crown ether constitution, which is believed to have the optimal ring size for stable 1:1 pseudorotaxane formation with DBA^+.[19] Although smaller crown ethers formed strong pseudorotaxane complexes with dialkylammonium salts,[20] for DBA^+ face-to-face bonding was observed[21] and larger crown ethers formed weaker complexes with DBA^+.[22]

In 2012, however, Wu and Dasgupta reported[23] that DBA^+ could also form 1:1 pseudo[2]rotaxane complexes with [23]crown ethers, much to the surprise of the scientific community. The [23]crown ethers utilized were 23C7H2 and 23C6H2, which neither possessed benzo-/naphtha- units nor had 8 oxygen atoms. This provides the impetus to further explore the utility of the supramolecular recognition motif, DBA^+-[23]crown ether analogues, in diverse fields. The synthesis of 23C7H2 and 23C6H2 typically requires three to four steps and involves the usage of a very expensive Grubbs catalyst, which might limit the practical application of these [23]crown ethers. Therefore, it is imperative to develop such a derivative of [23]crown ether which is inexpensive, easily synthesized, scalable and forms pseudo[2]rotaxane with the DBA^+ salt.

Herein, we report the synthesis of a [23]crown ether, *o*-xylene-capped 23-crown-7-ether (X23C7), in single step from commercially available starting materials, i.e., hexaethylene glycol (HEG) and *o*-xylylene dibromide, in good to excellent yield. As anticipated, the crown ether X23C7 formed pseudo[2]rotaxane complex with the DBA·PF_6 salt and exhibited a high association constant value (K_a = 2.6 × 10^3 M^{-1}). Subsequently, this affinity has been maneuvered for constructing the [2]catenane molecule 1-H·PF_6. The methodology involved threading-followed-by-ring-closing-metathesis,

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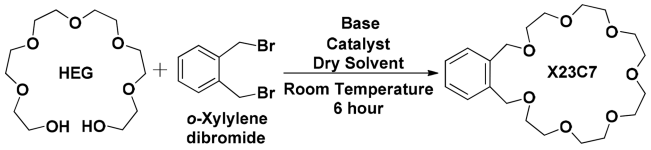
catalyzed by a Grubbs second generation catalyst. To the best of our knowledge, no prior application of supramolecular recognition motif, DBA^+-[23]crown ether, has been reported to date.

The optimized reaction conditions of X23C7 has been obtained by varying the solvent, bases, catalyst, and their equivalents (Table 1). Throughout, one equivalent of both

Table 1. Optimizing Conditions for X23C7[a]



entry	solvent	base (equiv)	catalyst (equiv)	yield (%)[b]
1	THF	NaH (3)	NIL	33
2	DMF	NaH (3)	NIL	37
3	ACN	NaH (3)	NIL	54
4	ACN	NaH (3)	KI (0.1)	64
5	ACN	NaH (3)	KI (0.2)	70
6	ACN	NaH (3)	KI (0.3)	73
7	ACN	NaH (3)	KPF_6 (0.1)	70
8	ACN	NaH (3)	KPF_6 (0.2)	79
9	ACN	NaH (3)	KPF_6 (0.25)	81
10	THF	NaH (3)	KPF_6 (0.2)	56
11	DMF	NaH (3)	KPF_6 (0.2)	60
12	DMF	KOH (2)	NIL	–[c]
13	DMF	K_2CO_3 (10)	NIL	–[c]

[a]100 mg scale of HEG has been used throughout. [b]Isolated yield. [c]No product formation could be detected at room temperature, and heating at 100 °C did not help.

HEG and *o*-xylylene dibromide has been used at room temperature. X23C7 has been designed such that the starting materials can undergo facile double *O*-alkylation at the reactive benzyl sites. The yields in entries 1 and 2 are very much comparable with that reported for DB24C8.[24] However, as per entry 3, acetonitrile (ACN) appears to be the best solvent choice for X23C7 synthesis. Thus, for increasing the percent yield, a template-directed approach has been investigated primarily in the acetonitrile solvent system. To exploit the K^+ template effect, KI (entries 4–6) and KPF_6 (entries 7–9) have been employed in the catalytic ratio. As can be seen from entries 4–9, the percent yield substantially increases, with the highest being 81% (entry 9). It is evident that KPF_6 is more effective than KI for the same equivalent. It is interesting to note that KI, which is one of the routinely available chemicals in laboratories, can also catalyze the reaction in pretty good yields (up to 73%, entry 6). Increasing the percentage equivalent of the catalyst from 10% to 20% results in higher enhancements of the percent yield of isolated X23C7. Thus, reactions with a 20% equivalent of KPF_6 were attempted in dry tetrahydrofuran (THF, entry 10) and dry dimethylformamide (DMF, entry 11), which resulted in substantial increase of yield to 56% and 60% respectively. Finally both KOH (entry 12) and K_2CO_3 (entry 13), expected to play the dual role of base and template, were tried and found to be ineffective. Ultimately, entry 9 was found to be the optimized reaction condition, and the same has been employed for synthesizing X23C7 on the gram scale. The yield however dropped to 78% which can still be considered an excellent yield, as this yield has been realized from commercially available chemicals. This yield is much higher than the earlier reported isolated yield of X23C7 (50%), prepared under heating conditions.[25]

The ability of X23C7 to form pseudo[2]rotaxane with $DBA\cdot PF_6$ was investigated by ^1H NMR spectroscopy and lower resolution ESI-MS. Pseudo[2]rotaxane $DBA\subset X23C7\cdot PF_6$ was obtained from the 1 mM equimolar mixture of $DBA\cdot PF_6$ and X23C7 in $CDCl_3$. The presence of complexed and uncomplexed species corresponding to both X23C7 and $DBA\cdot PF_6$ (Figure 1) suggests the pseudo[2]rotaxane formation

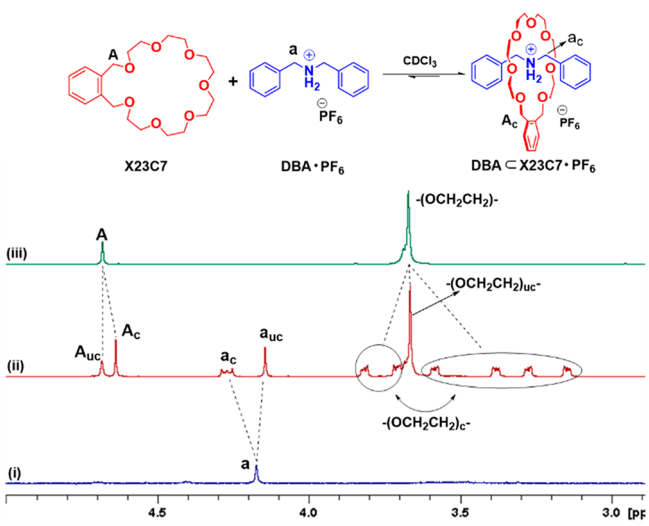


Figure 1. ^1H NMR ($CDCl_3$, 400 MHz) spectra of (i) $DBA\cdot PF_6$, (ii) 1:1 equimolar mixture of $DBA\cdot PF_6$ and X23C7, and (iii) X23C7. Dotted lines are drawn to indicate the presence of complexed and uncomplexed species, highlighting the formation of pseudo[2]-rotaxane $DBA\subset X23C7\cdot PF_6$.

is slow on the NMR time scale. Moreover, a strong peak corresponding to the 1:1 formation of the pseudo[2]rotaxane could be detected in the nominal ESI-MS spectrum (Figure S1 in the Supporting Information). The peaks corresponding to the $-(OCH_2CH_2)-$ protons of X23C7 showed a broad peak around 3.6 ppm, which on complexation with $DBA\cdot PF_6$ separated into six peaks of four protons each (Figure 1). Due to the complexation, both deshielding and shielding was observed for $-(OCH_2CH_2)-$ protons, with the chemical shifts ranging from 3.1 to 3.8 ppm. X23C7 is a symmetrical crown ether, and post complexation the appearance of $-(OCH_2CH_2)-$ protons into six equal sets of four protons indicates that the symmetry is still retained in the pseudo[2]-rotaxane $DBA\subset X23C7\cdot PF_6$. The association constant value was calculated using a single point NMR method and found to be $2.61 \times 10^3\ M^{-1}$ for the 1:1 pseudo[2]rotaxane complex, $DBA\subset X23C7\cdot PF_6$ (Figure S2). A comparison of association constant values of varied cavity sized crown ethers with DBA^+ in nonpolar media is available in the Supporting Information (Table S1).

Obviously, the next logical step would be to harness the utility of the DBA^+-X23C7 supramolecular synthon in MIMs. To achieve that, a diolefin-terminated linear thread comprising the DBA^+ moiety ($7\text{-}H\cdot PF_6$) has been prepared (Scheme 1). As depicted in Scheme 1, *p*-hydroxy benzaldehyde was alkylated with 11-bromo-1-undecene to give **2** in 97% yield. Boc protection of *p*-hydroxy benzylamine gave **3** in 67% yield. Compound **3** on alkylation with 11-bromo-1-undecene produced **4** in 51% yield, which on Boc deprotection resulted

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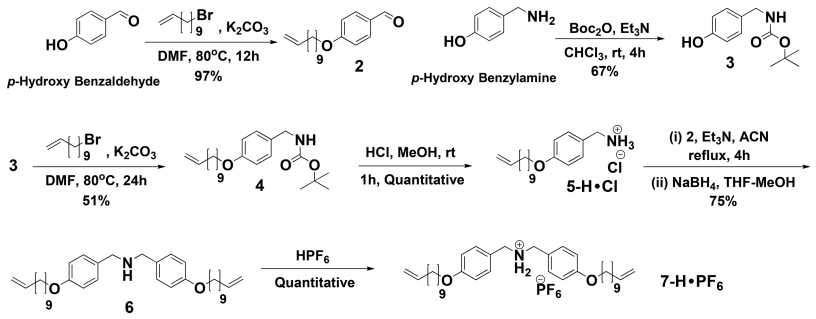
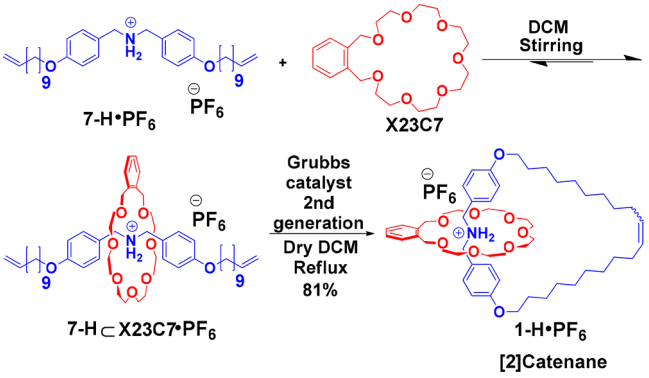
Scheme 1. Synthesis of Diolefin Terminated Thread 7-H·PF$_6$



in quantitative formation of the salt **5**-H·Cl. Compound **2** was condensed with 1 equiv of the salt **5**-H·Cl in the presence of triethylamine, which was subsequently reduced with sodium borohydride to give **6** in 75% yield. On protonation with HPF_6, compound 7-H·PF$_6$ was obtained in quantitative yield.

Subsequently, the salt 7-H·PF$_6$ was stirred with 5 equiv of X23C7 in dichloromethane to ensure complete conversion into the pseudo[2]rotaxane 7-H⊂X23C7·PF$_6$ (Scheme 2). This

Scheme 2. Synthesis of [2]Catenane 1-H·PF$_6$



threaded species has been subjected to ring-closing-metathesis, using a second generation Grubbs catalyst under refluxing conditions. The desired [2]catenane **1**-H·PF$_6$ was isolated as a mixture of *E* and *Z* isomers in excellent yield of 81%. Moreover, the excess 3 equiv of X23C7 has been isolated as well in pure form by column chromatography. This means that effectively 2 equiv of X23C7 was required for the synthesis of [2]catenane **1**-H·PF$_6$. The formation of [2]catenane, **1**-H·PF$_6$ can be confirmed from the stacked NMR spectra (Figure 2).

The observation of six equal sets of −(OCH$_2$CH$_2$)− protons of [2]catenane **1**-H·PF$_6$ (Figure 2ii), completely matches with that observed for the same set of protons of DBA⊂X23C7·PF$_6$ (Figure 1ii). The range of chemical shifts of the −(OCH$_2$CH$_2$)− protons is in the same region as well, i.e., 3.1−3.8 ppm. The downfield shift observed for benzylic protons "a" of the DBA$^+$ moiety (Figure 2ii) is also similar to that observed for the same set of protons of the pseudo[2]-rotaxane species, DBA⊂X23C7·PF$_6$. Such a downfield shift and splitting of benzylic protons of DBA$^+$ moiety is typically observed in interpenetrated geometries involving the crown ethers. The upfield shifts of benzylic protons "A" (of X23C7) in the [2]catenane **1**-H·PF$_6$ (Figure 2ii) again resembles the complexed peak of the same set of protons of the pseudo[2]rotaxane species, DBA⊂X23C7·PF$_6$ (Figure 1ii). The disappearance of terminal double bond peaks "c, d" and

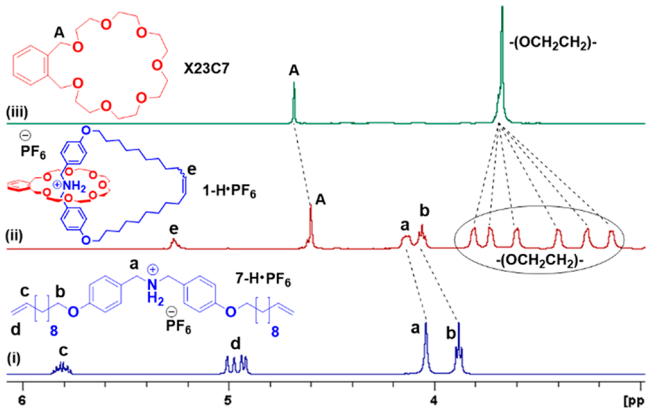


Figure 2. ^{1}H NMR (CDCl$_3$, 400 MHz) spectra of (i) 7-H·PF$_6$, (ii) [2]catenane **1**-H·PF$_6$, and (iii) X23C7. Dotted lines are drawn to indicate the upfield and downfield shifts, typically observed in MIMs.

appearance of broad substituted double bond peak "e" (Figure 2) are another indication of the formation of a mixture of *E* and *Z* isomers of the interlocked species **1**-H·PF$_6$.[10d] All of these observations clearly indicate that **1**-H·PF$_6$ has a [2]catenane topology, where X23C7 is encircling the DBA$^+$ moiety. The full ^{1}H NMR spectrum is available in the Supporting Information.

Additional evidence has been obtained from the 2D NOESY experiment, where strong NOE cross-peaks highlight the spatial interactions between X23C7 protons and DBA$^+$ protons in **1**-H·PF$_6$ (Figure S3). The −(OCH$_2$CH$_2$) protons of X23C7 show a strong correlation with the benzylic protons "a" and proximal benzene protons "b" of the DBA$^+$ moiety of the [2]catenane **1**-H·PF$_6$. Likewise, the NOE cross-peaks show a strong correlation of the benzylic protons of "A" of X23C7 with the benzylic protons "a" and proximal benzene protons "b" of the DBA$^+$ moiety of the [2]catenane **1**-H·PF$_6$.

Furthermore, HR ESI-MS of **1**-H·PF$_6$ showed a peak at *m*/*z* = 890.6139, corresponding to the species [M−PF$_6$]$^+$ (Figure 3). The observed *m*/*z* value is extremely close to the calculated mass of the species, which is 890.6141 (error 0.2 ppm). This observation indicates the purity of the isolated [2]catenane, **1**-H·PF$_6$. Next, we investigated the integrity of the **1**-H·PF$_6$ in the polar solvent by recording its ^{1}H NMR in DMSO-*d*$_6$ solvent. The room temperature ^{1}H NMR indicates complete retention of the topology as well as confirmation (of X23C7 encircling the DBA$^+$ moiety) of the [2]catenane. This observation further corroborates the formation of an interlocked geometry. Recording the ^{1}H NMR in DMSO-*d*$_6$ at increasing temperatures up to 353 K surprisingly did not alter the spectrum at all (Figure S4). While cooling back to

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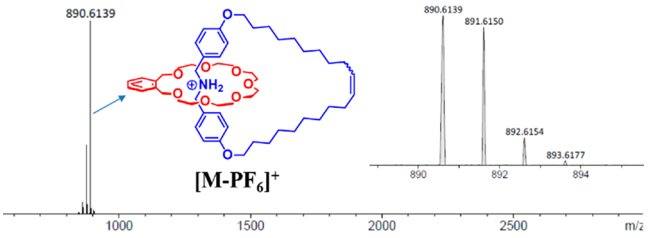

Figure 3. HR ESI-MS spectrum of the [2]catenane **1**·H·PF_6. The peak at m/z = 890.6139 corresponds to $[M-PF_6]^+$. The isotopic distribution also confirms the species is a monopositive cation.

room temperature, the spectra remained the same. Thus, the confirmation of X23C7 encircling the DBA^+ moiety in **1**·H·PF_6 is the thermodynamically most stable conformation, even at higher temperatures in a polar solvent system.

In conclusion, we have developed a facile, rapid, and high yielding (81%) synthesis of crown ether X23C7 in a single step from commercially available starting materials under room temperature condition. The template used for the synthesis involves readily available potassium-based salts such as KI and KPF_6. Gram scale synthesis has been achieved as well in 78% yield, which indicates the efficacy of the methodology developed. X23C7 has been found to form a pseudo[2]-rotaxane complex with DBA·PF_6, exhibiting a high association constant value (K_a = 2.6 × 10^3 M^{-1}). Following the footsteps of DBA^+-DB24C8, the supramolecular synthon DBA^+-X23C7 has been employed for the synthesis of the [2]catenane **1**·H·PF_6 by ring-closing-metathesis (RCM). The extremely good yield (81%) of the isolated [2]catenane, **1**·H·PF_6, is very encouraging for the onset of X23C7 in the field of MIMs. Looking at the success of the supramolecular synthon DBA^+-DB24C8, the future of X23C7 seems bright. Since it is established that the crown ether X23C7 can pass over the benzene moieties, other axles like BPE^{2+},[26] *N*-benzylanilinium,[10f] and benzimidazolium[27] may well be exploited with X23C7 for pseudo[2]rotaxane complex formation. X23C7 is not only a cheaper alternative to DB24C8 but also a valuable addition to the crown ether family for supramolecular and MIM-based switch fabrication. The properties of X23C7, and chemistry of other smaller crown ethers in supramolecular and MIM systems, are currently under investigation in our laboratory.

EXPERIMENTAL SECTION

General Information. All reagents and starting materials were bought from commercial suppliers and used without further purification. Anhydrous dichloromethane (DCM) was obtained from dry distillation of its analytical grade by refluxing over CaH_2. Anhydrous tetrahydrofuran (THF) was obtained by distilling its analytical grade by refluxing over sodium-benzophenone. Anhydrous acetonitrile and DMF were purchased from CDH. Freshly distilled dry solvents were always used. Column chromatography was performed on silica gel (100−200 mesh). Deuterated solvents (Sigma-Aldrich) for NMR spectroscopic analyses were used as received. All NMR spectra were recorded on a Bruker 400 MHz FT-NMR spectrometer or Bruker Avance-III 500 MHz NMR spectrometer. All chemical shifts are quoted in ppm with multiplicities being denoted by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Mass spectra were recorded in ESI mode on a Maxis Impact instrument (Bruker).

*Synthesis of 4-(Undec-10-en-1-yloxy)benzaldehyde (**2**).* A mixture of 4-hydroxybenzaldehyde (1 g, 8.2 mmol), 11-bromo-1-undecene (2.3 g, 9.8 mmol), and K_2CO_3 (3.4 g, 24.6 mmol) in DMF (25 mL) was heated to 80 °C in an oil bath under nitrogen atmosphere for 12 h. The mixture was filtered to remove undissolved excess K_2CO_3. The solvent was removed in vacuum to leave a residue which was extracted with $CHCl_3$. The organic layer was washed with water and dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum. The crude residue was purified by column chromatography (silica gel, EA/hexane = 1:9) to give compound **2** as a yellow oil (2.19 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 9.87 (s, 1H, CHO), 7.83 (d, J = 8.6 Hz, 2H, Ar), 6.99 (d, J = 8.6 Hz, 2H, Ar), 5.86−5.75 (m, 1H, C(H)=CH_2), 5.01−4.91 (m, 2H, CH = C(H_2)), 4.03 (t, J = 6.52 Hz, 2H, CH_2), 2.06−2.01 (m, 2H, CH_2), 1.84−1.77 (m, 2H, CH_2), 1.47−1.29 (br, 12H, CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ ppm = 190.7, 164.2, 139.1, 131.9, 129.7, 114.7, 114.1, 68.4, 33.7, 29.47, 29.40, 29.3, 29.09, 29.05, 28.9, 25.9. HR MS (ESI): m/z Calcd for $C_{18}H_{27}O_2$ $(M + H)^+$: 275.2006, found 275.2010.

*Synthesis of tert-Butyl 4-Hydroxybenzylcarbamate (**3**).* 4-Hydroxybenzylamine (0.5 g, 4.06 mmol) was dissolved in AR grade $CHCl_3$ (25 mL) under nitrogen atmosphere. To this, triethylamine (0.62 g, 6.09 mmol) was added and stirred for 5 min. This was followed by addition of Boc_2O (1.33 g, 6.09 mmol), and the reaction mixture was stirred for 4 h. The solvent was removed under vacuum, leaving the crude residue which was purified by column chromatography (silica gel, EA/hexane = 2:8) to give compound **3** as a colorless oil (0.61 g, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 7.14 (d, J = 7.9 Hz, 2H, Ar), 6.78 (d, J = 8.2 Hz, 2H, Ar), 5.23 (s, 1H, −OH), 4.78 (s, 1H, -NH), 4.23 (br, 2H, CH_2), 1.45 (s, 9H, CH_3). ^{13}C{^{1}H} NMR (125 MHz): δ ppm = 156.0, 155.1, 130.7, 128.9, 115.4, 79.6, 44.1, 28.4. HR MS (ESI): m/z Calcd for $C_{12}H_{17}NO_3Na$ $(M + H)^+$: 224.1281, found 224.1274.

*Synthesis of tert-Butyl 4-(Undec-10-en-1-yloxy)benzylcarbamate (**4**).* A mixture of compound **3** (0.6 g, 2.69 mmol), 11-bromo-1-undecene (0.752 g, 3.23 mmol), and K_2CO_3 (1.12 g, 8.07 mmol) in DMF (20 mL) was heated to 80 °C in an oil bath under nitrogen atmosphere for 24 h. The mixture was filtered to remove undissolved excess K_2CO_3. The solvent was removed in vacuum to leave a residue which was extracted with $CHCl_3$. The organic layer was washed with water and dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum. The crude residue was purified by column chromatography (silica gel, EA/hexane = 1:9) to give compound **4** as a yellow oil (0.513 g, 51%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 7.19 (d, J = 8.3 Hz, 2H, Ar), 6.85 (d, J = 8.5 Hz, 2H, Ar), 5.86−5.75 (m, 1H, C(H)=CH_2), 5.01−4.91 (m, 2H, CH = C(H_2)), 4.76 (br, 1H, -NH), 4.23 (br, 2H, CH_2), 3.92 (t, J = 6.5 Hz, 2H, CH_2), 2.06−2.01 (m, 2H, CH_2), 1.79−1.72 (m, 2H, CH_2), 1.45 (s, 9H, CH_3), 1.37−1.29 (br, 12H, CH_2). ^{13}C{^{1}H} NMR (100 MHz): δ ppm = 158.4, 155.8, 139.2, 130.8, 128.8, 114.5, 114.1, 79.3, 68.0, 44.2, 33.8, 29.4, 29.3, 29.1, 28.9, 28.4, 26.0. HR MS (ESI): m/z Calcd for $C_{23}H_{37}NO_3Na$ $(M + Na)^+$: 398.2666, found 398.2656.

*Synthesis of (4-(Undec-10-en-1-yloxy)phenyl)methanaminium chloride (**5**·H·Cl).* Compound **4** (0.513 g, 1.37 mmol) was dissolved in MeOH (50 mL, 0.03 M) under nitrogen. A volume of 30 mL of ∼2 M HCl was added under nitrogen and stirred for 1 h. The excess reagent and solvent were removed under vacuum to obtain compound **5**·H·Cl as a white amorphous solid in quantitative yield. ^{1}H NMR (500 MHz, DMSO): δ ppm = 8.19 (br, 3H, NH_3^+), 7.36 (d, J = 8.4 Hz, 2H, Ar), 6.93 (d, J = 8.4 Hz, 2H, Ar), 5.80−5.72 (m, 1H, C(H) =CH_2), 4.98−4.90 (m, 2H, CH = C(H_2)), 3.94−3.91 (br, 4H, CH_2), 2.00−1.96 (m, 2H, CH_2), 1.69−1.64 (m, 2H, CH_2), 1.37−1.22 (br, 12H, CH_2). ^{13}C{^{1}H} NMR (125 MHz): δ ppm = 159.2, 139.2, 130.9, 126.0, 115.7, 115.1, 114.9, 67.9, 61.2, 42.2, 33.5, 32.8, 29.3, 29.1, 28.8, 28.6, 25.8. HR MS (ESI): m/z Calcd for $C_{18}H_{30}NO$ $(M - Cl)^+$: 276.2322, found 276.2300.

*Synthesis of **6**.* Compound **5**·H·Cl (0.3 g, 0.96 mmol), compound **2** (0.26 g, 0.96 mmol), and triethylamine (0.097 g, 0.96 mmol) were mixed in CH_3CN (20 mL) under nitrogen. The suspension was stirred for 45 min and then refluxed for another 4 h in an oil bath. The reaction mixture was allowed to cool before removing the solvent under vacuum. The white residue was dissolved in THF (20 mL) and MeOH (20 mL) to which $NaBH_4$ (0.24 g, 6.3 mmol) was added in

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portions. After stirring for overnight, the solvent was removed under vacuum, leaving a residue which was extracted by $CHCl_3$. The organic layer was washed with brine and dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum leaving the crude residue which was purified by column chromatography (silica gel, MeOH/DCM = 1:9) to give compound **6** as light a yellow oil (0.384 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 7.16 (d, J = 8.4 Hz, 4H, Ar), 6.76 (d, J = 8.5 Hz, 4H, Ar), 5.76−5.66 (m, 2H, C(H)=CH_2), 4.92−4.82 (m, 4H, CH = C(H_2)), 3.82 (t, J = 6.5 Hz, 4H, CH_2), 3.62 (s, 4H, CH_2), 1.97−1.92 (m, 4H, CH_2), 1.69−1.62 (br, 4H, CH_2), 1.34−1.20 (br, 24H, CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ ppm = 158.4, 139.2, 130.3, 129.7, 114.4, 114.1, 68.0, 51.7, 33.8, 29.5, 29.4, 29.3, 29.1, 28.9, 26.0. HR MS (ESI): *m*/*z* Calcd for $C_{36}H_{56}NO_2$ $(M + H)^+$: 534.4306, found 534.4302.

Synthesis of 7-H·PF$_6$. Compound **6** (0.412 g, 0.77 mmol) was dissolved in methanol (10 mL), and then 2 mL of HPF_6 acid solution (~55 wt % in H_2O) was added to precipitate out the salt 7-H·PF_6. The precipitate was filtered off, washed with water, and dried over vacuum to give 7-H·PF_6 as white amorphous solid in quantitative yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ ppm = 7.24 (br, 4H, Ar), 6.89 (d, J = 8.5 Hz, 4H, Ar), 6.59 (br, 2H, NH_2^+), 5.85−5.76 (m, 2H, C(H)=CH_2), 5.00−4.91 (m, 4H, CH = C(H_2)), 4.04 (s, 4H, CH_2), 3.88 (t, J = 6.5 Hz, 4H, CH_2), 2.05−2.01 (m, 4H, CH_2), 1.76−1.68 (br, 4H, CH_2), 1.40−1.29 (br, 24H, CH_2). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ ppm = 160.5, 139.2, 131.3, 120.5, 115.4, 114.1, 68.1, 50.4, 33.8, 29.7, 29.5, 29.4, 29.3, 29.15, 29.13, 28.9, 26.0. HR MS (ESI): *m*/*z* Calcd for $C_{36}H_{56}NO_2$ $(M\text{-}PF_6)^+$: 534.4306, found 534.4306.

Optimized Procedure for the Synthesis of X23C7. NaH (60%, 0.04 g, 1.064 mmol) was suspended in 5 mL of dry acetonitrile (0.07 M) under nitrogen. To the suspended solution, hexaethylene glycol (0.1 g, 0.354 mmol) was added in portions and stirred for 10 min. Next KPF_6 (0.016 g, 0.0885 mmol) was added to the solution. Subsequently, *o*-xylylenedibromide (0.093 g, 0.354 mmol) was added to the reaction mixture and stirred for 6 h at room temperature. The solvent was removed in vacuum to leave a residue which was extracted with $CHCl_3$. The organic layer was washed with water and dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum. The crude residue was purified by column chromatography (silica gel, Acetone/Hexane = 1:3) to give X23C7 as a colorless oil (0.113 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 7.38 (br, 2H, Ar), 7.27 (br, 2H, Ar), 4.68 (s, 4H, CH_2), 3.67 (br, 24H, OCH_2CH_2). ^{13}C{^{1}H} NMR (100 MHz, CDCl3): δ ppm = 136.7, 129.0, 127.7, 71.1, 70.8, 70.74, 70.71, 70.6, 69.7. HR MS (ESI): *m*/*z* Calcd for $C_{20}H_{32}O_7Na$ $(M + Na)^+$: 407.2040, found 407.2043.

Optimized Procedure for the Synthesis of X23C7 on a Gram Scale. NaH (0.44 g, 11 mmol) was suspended in 50 mL of dry acetonitrile (0.07 M) under nitrogen. To the suspended solution, hexaethylene glycol (1.02 g, 3.61 mmol) was added in portions and stirred for 10 min. Next KPF_6 (0.16 g, 0.90 mmol) was added to the solution. Subsequently, *o*-xylylenedibromide (0.96 g, 3.63 mmol) was added to the reaction mixture and stirred for 6 h at room temperature. The solvent was removed in vacuum to leave a residue which was extracted with $CHCl_3$. The organic layer was washed with water and dried over anhydrous Na_2SO_4, and the solvent was then removed under vacuum. The crude residue was purified by column chromatography (silica gel, acetone/hexane = 1:3) to give X23C7 as a colorless oil (1.08 g, 78%).

Synthesis of [2]Catenane, 1-H·PF$_6$. Compound 7-H·PF_6 (0.1 g, 0.148 mmol) and X23C7 (0.284 g, 0.74 mmol) were dissolved in 10 mL of DCM solvent and stirred for 24 h, and then the solvent was removed under vacuum without heating. The residue (7-H⊂X23C7·PF_6) was dissolved in dry DCM (400 mL, 0.0003 M) under nitrogen atmosphere. A second generation Grubbs catalyst (0.012 g, 0.0148 mmol) was added, and the resulting mixture was refluxed for 60 h in an oil bath. The reaction mixture was cooled, followed by quenching with ethyl vinyl ether. The excess solvent was removed in vacuum, and the residue was subjected to column chromatography (silica gel: acetone/hexane = 2:3 (v/v)) to isolate the excess (3 equiv) X23C7 (0.172 g), followed by another column chromatography (silica gel: Acetone/$CHCl_3$ = 5:95) to give the desired product **1**-H·PF_6 as a yellow color gum (0.123 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm = 7.34 (br, 2H, Ar), 7.22 (d, J = 8.3 Hz, 4H, Ar), 7.16 (br, 2H, Ar), 6.88 (d, J = 8.3 Hz, 4H, Ar), 5.26 (br, 2H, C(H)=C(H)), 4.60 (s, 4H, CH_2), 4.13 (br, 4H, CH_2), 4.05 (br, 4H, CH_2), 3.81 (br, 4H, OCH_2CH_2), 3.73 (br, 4H, OCH_2CH_2), 3.60 (br, 4H, OCH_2CH_2), 3.40 (br, 4H, OCH_2CH_2), 3.25 (br, 4H, OCH_2CH_2), 3.14 (br, 4H, OCH_2CH_2), 1.86 (br, 4H, CH_2), 1.70 (br, 4H, CH_2), 1.39 (br, 4H, CH_2), 1.24−1.16 (br, 20H, CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ ppm = 159.6, 135.3, 131.5, 130.2, 129.8, 128.2, 123.7, 114.9, 114.8, 71.5, 71.0, 70.9, 70.7, 70.5, 67.5, 51.2, 32.4, 29.6, 29.4, 29.3, 29.2, 28.8, 28.7, 28.2, 25.5. HR MS (ESI): *m*/*z* Calcd for $C_{54}H_{84}NO_9$ $(M - PF_6)^+$: 890.6141, found 890.6139.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00674.

Details on the characterization of all new compounds; ^{1}H NMR, ^{13}C NMR, 2D NOESY NMR, nominal ESI-MS, and VT NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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