*Mechanically Interlocked Compounds*

# The Exclusivity of Multivalency in Dynamic Covalent Processes**

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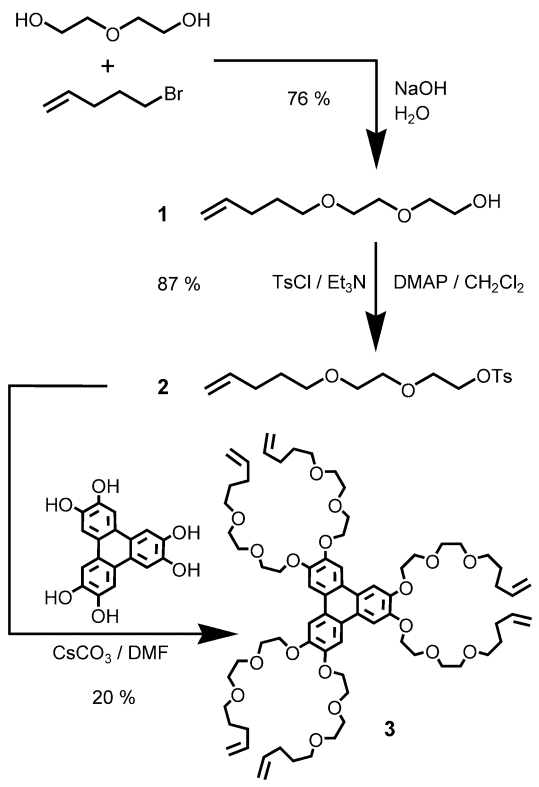
Nature's reliance on multivalency[1] as a means[2] of compensating for weak monovalent protein–ligand interactions is now a widely accepted phenomenon[3] which controls a panoply of biological events and whose delicate manipulations could have far-reaching therapeutic implications. In recent times, the physical basis of multivalency effects, based on a thermodynamic model combined with computational studies, has been explored rigorously[4] and a comprehensive thermodynamic investigation of the calcium–EDTA interactions has been reported.[5] Since thermodynamics seem, by and large,[6] to rule the roost as far as multivalency is concerned, it occurred to us that it should be the perfect phenomenon to probe using the concept of dynamic covalent chemistry.[7] Herein we describe a situation in which the concept works in the exclusive context of the phenomenon; that is, dynamic covalent chemistry can be achieved in a highly efficient manner using multivalent ligands, but fails altogether when no ligand or a monovalent counterpart is employed.

As a part of some on-going research to probe multivalency in artificial systems[8] exhibiting molecular recognition, we have recently uncovered a compelling example[9] of multivalency between a tritopic receptor, in which three benzo[24]crown-8 rings are fused onto a triphenylene core, and a trifurcated trication, wherein three dibenzylammonium ions are linked 1,3,5 to a central benzenoid core: the outcome is an extremely stable ($K_a > 10^7\ mol\,L^{-1}$ in $CH_2Cl_2$) triply threaded, two-component superbundle. This observation led subsequently to the template-directed synthesis[10] of a prototype[11] of an artificial molecular machine,[12] namely, a mechanically interlocked, triply threaded, molecular bundle by kinetically controlled post-assembly covalent modification. The advent of dynamic covalent chemistry[7] has, however, opened up an attractive alternative route[13] to mechanically interlocked molecules which relies upon the thermodynamically controlled strict self-assembly of their covalently linked components proceeding in unison with mechanical bond formation under the guidance of the templation provided by noncovalent interactions. In particular, it has been shown that 1) the reversible ring-closing metathesis (RCM) reaction and 2) the ring-opening, ring-closing metathesis (RORCM) reaction, also operating under equilibrium control, are both mediated by functional-group-tolerant ruthenium–alkylidene catalysts[14] and can be used[15] in the thermodynamically controlled synthesis of catenanes and rotaxanes.[16] In the specific knowledge that [2]rotaxanes[17] and [3]catenanes,[18] where the supramolecular assistance[19] for their formation comes from the interaction[20] of $CH_2NH_2^+CH_2$ ion centers, either by developing olefinic crown ether analogues containing 24-membered rings or with dibenzo[24]crown-8, we decided to explore the possibility that the multivalency effect can be exploited during RCM and RORCM. We demonstrate that it can be exploited in a convincing manner: multivalency flourishes in situations where monovalency falters.

As outlined in Schemes 1 and 2, respectively, we have prepared the triphenylene hexa-olefin **3** and the trifurcated trisammonium salt [**5**-$H_3$][$PF_6$]$_3$ by standard protocols (see the Experimental Section). Their $^1$H NMR spectra, recorded in $CD_3CN$ and $CDCl_3$, respectively, are reproduced in Figure 1 a and b, respectively. When a solution of **3** (15 mM) in $CD_2Cl_2$ at




***Scheme 1.*** Synthesis of the hexa-olefin **3**. DMAP = 4-dimethylaminopyridine, DMF = dimethylformamide, Ts = toluene-4-sulfonyl.

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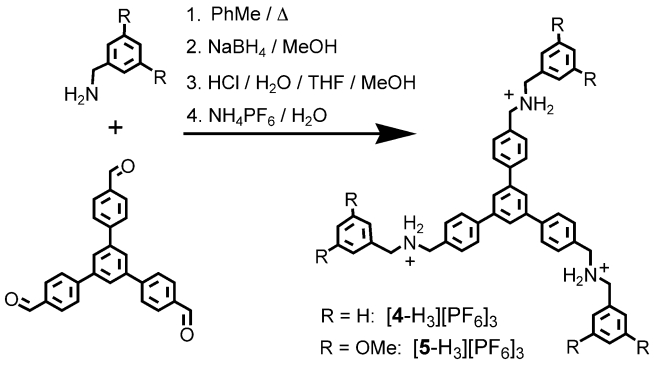



***Scheme 2.*** Syntheses of the trisammonium tris(hexafluorophosphate) salts [**4**-$H_3$][$PF_6$]$_3$ and [**5**-$H_3$][$PF_6$]$_3$. THF = Tetrahydrofuran

40 °C is treated with [$(PCy_3)_2(Cl)_2Ru$=CHPh] (1.6 mM, 11 mol %), a complex mixture of products is formed, as indicated by thin layer chromatography and $^1$H NMR spectroscopy. A very similar outcome emerged when a mixture of **3** (15 mM) with the monovalent bis-3,5-dimethoxybenzylammonium hexafluorophosphate[17] (45 mM) was treated under exactly the same reaction conditions with the same ruthenium–alkylidene catalyst. Thus, both without and with a monovalent template, little or none of the desired crown ether analogue **7**, or the anticipated[4] rotaxane, are formed. The reasons for these observations could relate to the myriad of potential products that could be formed by different intramolecular RCM reactions. Also, amplification by the monovalent template to give a [4]rotaxane would incur a considerable entropy loss which most likely would swamp a very small enthalpic gain.

When a mixture (each 15 mM in $CD_2Cl_2$ at 40 °C) of **3** and [**5**-$H_3$][$PF_6$]$_3$ was subjected to a RCM reaction using [$(PCy_3)_2(Cl)_2Ru$=CHPh] (1.6 mM, 11 mol %), the $^1$H NMR spectrum recorded after 4 h revealed a complex array of well-defined resonances. With the aid of 2D NMR ($^1$H-$^1$H COSY) experiments, almost all the resonances could be assigned to an isomeric mixture of [**6**-$H_3$][$PF_6$]$_3$ containing C=C double bonds with both *E* and *Z* configurations. The formation (Scheme 3) of the mechanically interlocked molecular "bundle" [**6**-$H_3$][$PF_6$]$_3$ with averaged quasi $C_{3v}$ symmetry is consistent with the $^1$H NMR spectroscopic data (see Figure 1c). The methylene protons $H_d$ and $H_e$ on the carbon atoms adjacent to the secondary dialkylammonium centers in [**6**-$H_3$][$PF_6$]$_3$ resonate as broad multiplets centered on $\delta = 4.63$ and 4.74 ppm: these "same" protons resonate as sharp singlets at $\delta = 4.20$ and 4.29 ppm in [**5**-$H_3$][$PF_6$]$_3$. The downfield shifts and the multiplicities exhibited by $H_d$ and $H_e$ in [**6**-$H_3$][$PF_6$]$_3$ are diagnostic of their having been threaded by benzo[24]-crown-6 rings, that is, they demonstrate the interlocked nature of the "two" components in [**6**-$H_3$]$^{3+}$. Furthermore, the resonances of the aromatic core protons $H_a$ and $H_h$ at $\delta =$ 7.72 and 7.44 ppm, respectively, in the "two" components within [**6**-$H_3$]$^{3+}$ are shifted significantly upfield relative (Figure 1a and b) to the chemical shifts ($\delta = 7.96$ and 7.88 ppm, respectively) of the analogous protons in the individual components—namely [**5**-$H_3$]$^{3+}$ and **3**, respectively—which indicates π-π stacking of the central aromatic cores of the components with respect to one another. The

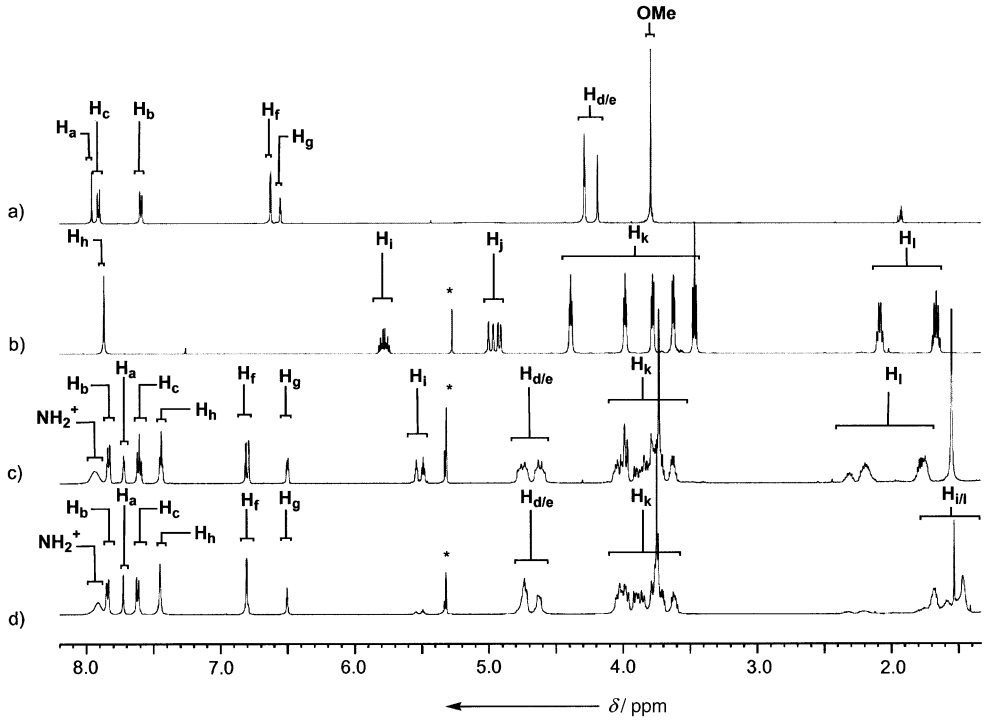
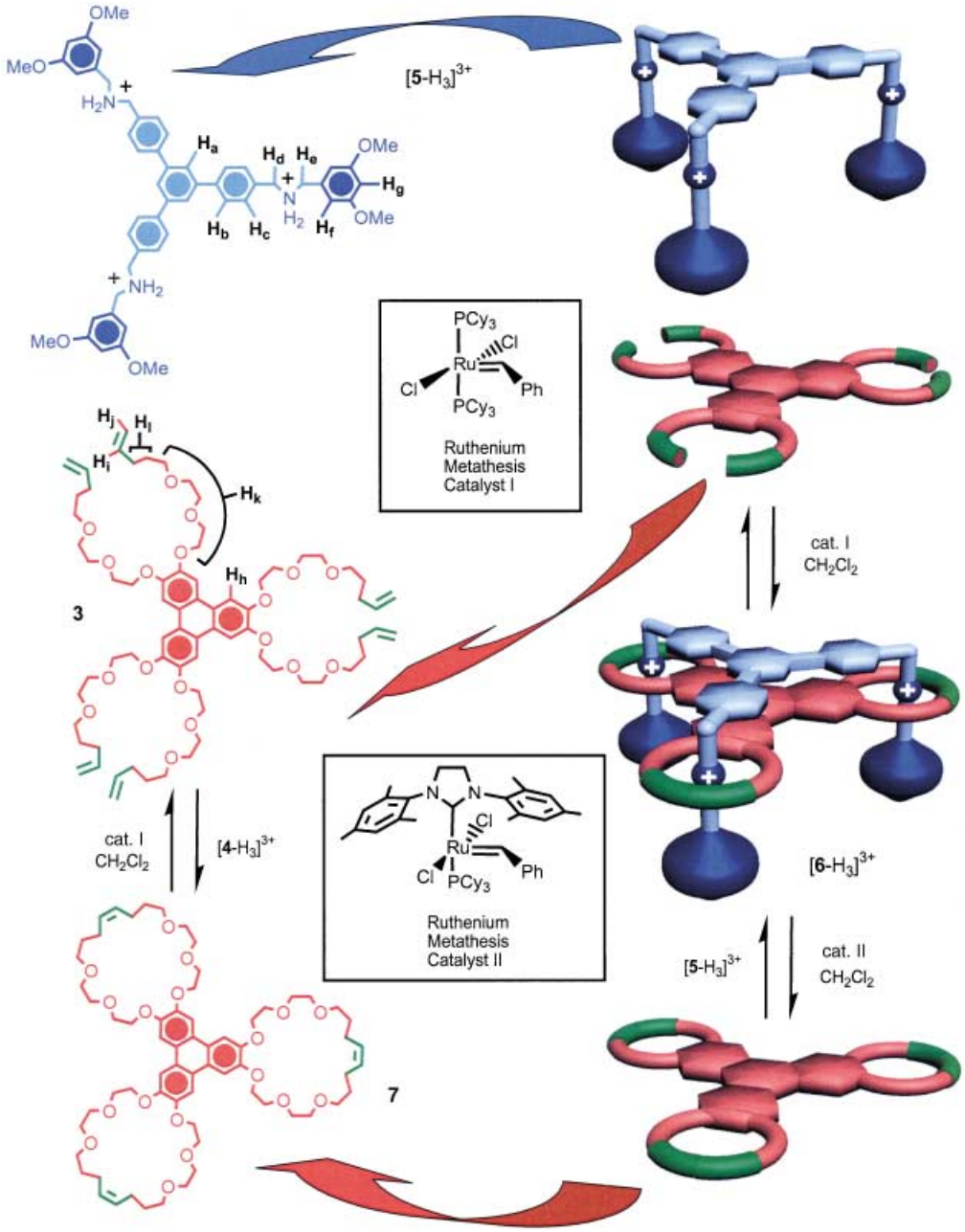



***Figure 1.*** The $^1$H NMR spectra (500 MHz, 298 K) of a) the trifurcated trisammonium salt [**5**-$H_3$][$PF_6$]$_3$ (15 mM in $CD_3CN$), b) the hexa-olefin **3** (15 mM in $CDCl_3$), c) the mechanically interlocked "bundle" [**6**-$H_3$][$PF_6$]$_3$ (15 mM in $CD_2Cl_2$), and d) the hydrogenated [**6**-$H_3$][$PF_6$]$_3$ (15 mM in $CD_2Cl_2$). Asterisk = residual solvent.




***Scheme 3.*** The efficient preparation of the mechanically interlocked "bundle" [**6**-$H_3$][$PF_6$]$_3$ as a mixture of isomers containing C=C bonds with both *E* and *Z* configurations can be achieved through either a ring-closing metathesis (RCM) reaction starting from an equimolar mixture (each 15 mM in $CH_2Cl_2$ at 40 °C) of the trifurcated trisammonium salt [**5**-$H_3$][$PF_6$]$_3$ and hexa-olefin **3** using the functional group tolerant [$(PCy_3)_2(Cl)_2Ru$=CHPh] (1.6 mM, 11 mol%) catalyst or ring-closing ring-opening metathesis (RORCM) reaction starting from an equimolar mixture (each 16 mM in $CH_2Cl_2$ at 25 °C) of the trifurcated trisammonium salt [**5**-$H_3$][$PF_6$]$_3$ and triscrown **7** using the catalyst [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh] (2.35 mM, 15 mol%). The synthesis of the triscrown **7** is shown on the left side. A triply threaded two component "superbundle" is assembled from an equimolar mixture (25 mM each in $CH_2Cl_2$ at 40 °C) of **3** and the trifurcated trisammonium tris(hexafluorophosphate) salt [**4**-$H_3$][$PF_6$]$_3$ containing [$(PCy_3)_2(Cl)_2Ru$=CHPh] (1.6 mM, 6 mol%) as the catalyst. The 1:1 complex formed as a result of this RCM reaction was then treated with a slight excess (>3 equiv) of $Et_3N$ to deprotonate the [**4**-$H_3$]$^{3+}$ component and so release[9] the tris(crown ether) **7** as a mixture of isomers where the C=C bonds in the macrorings have either *E* or *Z* configurations.

almost quantitative production[21] of [**6**-$H_3$][$PF_6$]$_3$ is presumably the result of the build-up of cooperative binding interactions, which result from the three productive RCM reactions that lead to the statistical and cluster effects[8] associated with the multivalency that characterizes the thermodynamically stable product. Hydrogenation ($H_2$/$PtO_2$) of all the (*E*/*Z*) olefinic bonds present in [**6**-$H_3$][$PF_6$]$_3$ yielded (72%) a mechanically interlocked bundle with averaged $C_{3v}$ symmetry as evidenced (Figure 1d) by $^1$H NMR spectroscopy. The "resonance" at $\delta = 5.53$ ppm for the olefinic protons $H_i$ in [**6**-$H_3$][$PF_6$]$_3$ disappears and is replaced by a signal centered on $\delta = 1.57$ ppm for protons

associated with $CH_2$ groups located in the middle of polymethylene chains.

We have also discovered that it is possible to assemble [**6**-$H_3$][$PF_6$]$_3$ directly from the situation (Scheme 3) wherein both components—that is, [**5**-$H_3$]$^{3+}$ and **7**—are already preformed. The tris(crown ether) **7** was synthesized by, first of all, constructing a triply threaded two-component "superbundle" from an equimolar mixture (25 mM each in $CH_2Cl_2$ at 40 °C) of **3** and the trifurcated trisammonium tris(hexafluorophosphate)[9] salt [**4**-$H_3$][$PF_6$]$_3$ containing [($PCy_3$)$_2$($Cl$)$_2$Ru=CHPh] (1.6 mM, 6 mol %) as the catalyst. The 1:1 complex formed as a result of this RCM reaction was then treated with a slight excess (> 3 equiv) of $Et_3N$ to deprotonate the [**4**-$H_3$]$^{3+}$ component and so release[9] the tris(crown ether) **7** as a mixture of isomers in which the C=C bonds in the macrorings have either *E* or *Z* configurations. The "compound" was isolated in 69 % yield following chromatography. Hydrogenation ($H_2$/$PtO_2$) of the C=C bonds in **7** afforded a *pure* saturated tris(crown ether) which was fully characterized by $^1$H NMR spectroscopy and mass spectrometry. Next, a solution of [**5**-$H_3$]$^{3+}$ and **7**—each 16 mM in $CD_2Cl_2$—was prepared and an $^1$H NMR spectrum was recorded (Figure 2).

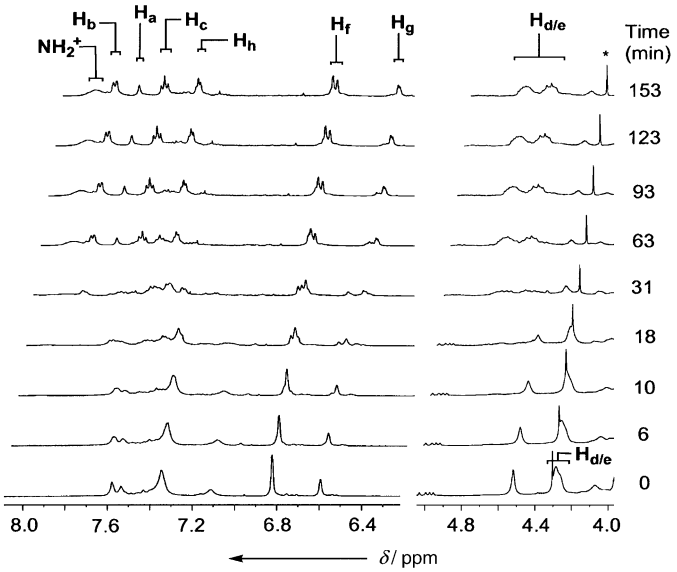



***Figure 2.*** Partial $^1$H NMR spectra (500 MHz, $CD_2Cl_2$, 16 mM each, 298 K) of an equimolar mixture of [**5**-$H_3$][$PF_6$]$_3$ and **7**, before (0 min) and after (6–153 min) addition of the catalyst [($IMesH_2$)($PCy_3$)($Cl$)$_2$Ru=CHPh] (2.35 mM, 15 mol %), which shows the exclusive formation (> 95 %) of the mechanically interlocked "bundle" [**6**-$H_3$][$PF_6$]$_3$ with time in a series of RORCM reactions. Asterisk = residual solvent.

It revealed that, even though the two components do *not* form a supramolecular bundle, an RORCM reaction does take place upon addition of [($IMesH_2$)($PCy_3$)($Cl$)$_2$Ru=CHPh] (2.3 mM, 15 mol %) as the catalyst.[22] The equilibration process was followed (Figure 2) by $^1$H NMR spectroscopy: equilibrium was attained in about 150 minutes to give a 95 % yield of the mechanically interlocked two-component "bundle" [**6**-$H_3$][$PF_6$]$_3$ which was also characterized by mass spectrometry. Hence, an RCM reaction has been employed, using a template, to make a component—namely, the tris(crown ether) **7**—for use subsequently in a successful RORCM reaction, using another template, to make a "bundle" incorporating that component.

Since the multivalency effect[1–6] is primarily a thermodynamic phenomenon, it seems entirely reasonable that multivalent sites between two or more components can be created spontaneously in situ by dynamic covalent chemistry,[7] a concept wherein reactivity is expressed in a thermodynamic context. The results reported here, together with those already described in the literature,[9,10] demonstrate that it is much less efficient to synthesize both components of a multivalent recognition site separately than it is to use one multivalent component to act as a template for the catalytically orchestrated construction of the other component. The situation is reminiscent of nature which frequently uses enzymes, in conjugation with self-assembly processes, to build up large and functional molecular structures. We foresee developments in polymer chemistry where the dynamic interplay between molecular recognition and the reversible formation of covalent (and mechanical) bonds using suitable catalysts will lead to the efficient production of high-molecular-weight polymers just as rich in information content as are many biopolymers.

## *Experimental Section*

**1**: A solution of diethylene glycol (71 g, 0.67 mol), 5-bromo-1-pentene (10 g, 0.17 mol) in $H_2O$ containing NaOH (13.4 g, 0.33 mol) was heated at 80 °C for 24 h. A standard work-up procedure gave a crude product, which was purified by column chromatography ($SiO_2$:hexanes/$Et_2O$, 1:1), to yield **1** as a colorless oil (11.7 g, 76 %). $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 1.64$ (m, 2H), 2.05 (m, 2H), 3.42 (m, 2H), 3.61 (m, 8H), 4.94 (m, 2H), 5.74 ppm (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 28.5$, 30.0, 61.5, 70.0, 70.2, 70.6, 72.4, 114.6, 138.0 ppm.

**2**: Compound **1** (3.0 g, 17.0 mmol), $Et_3N$ (8.6 g, 85.0 mmol), and a few crystals of DMAP were dissolved in dry $CH_2Cl_2$ (50 mL) and a solution of TsCl (7.0 g, 36.0 mmol) in dry $CH_2Cl_2$ (100 mL) was added over 2 h. The reaction mixture was stirred overnight before being subjected to a standard work-up procedure. Column chromatography ($SiO_2$, hexanes/$Et_2O$, 1:1) of the crude product afforded **2** as a pale yellow oil (4.9 g, 87 %). $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 1.63$ (m, 2H), 2.06 (m, 2H), 2.42 (s, 3H), 3.41 (t, $J = 7$ Hz, 2H), 3.48 (m, 2H), 3.55 (m, 2H), 3.67 (t, $J = 5$ Hz, 2H), 4.14 (t, $J = 5$ Hz, 2H), 4.94 (m, 2H), 5.77 (m, 1H), 7.31 (d, $J = 8$ Hz, 2H), 7.77 ppm (d, $J = 8$ Hz, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 21.5$, 28.6, 30.1, 68.5, 69.1, 69.9, 70.6, 70.7, 114.6, 127.8, 129.7, 132.9, 138.1, 144.7 ppm. HRMS (EI): *m/z* found: 329.1425, calcd for $C_{14}H_{25}O_5S$: 329.1423 [$M$+H]$^+$.

**3**: An oven-dried 1 L three-necked, round-bottomed flask, equipped with a stirrer bar, a gas-inlet tube, a dropping funnel, and a condenser, was purged with Ar for 10 min and then filled with anhydrous DMF (150 mL). $Cs_2CO_3$ (10.1 g, 31.0 mmol) was added to the flask and the white suspension stirred vigorously with heating at 100 °C. The dropping funnel was charged with a solution of 2,3,6,7,10,11-hexahydroxytriphenylene (500 mg, 1.6 mmol) and **2** (4.1 g, 12.4 mmol) in anhydrous DMF (250 mL) and this solution was added dropwise over 24 h to the suspension, which was then heated at 100 °C for another 3 days. On cooling the reaction mixture down to room temperature, the suspension was filtered off and the residue was washed with $CHCl_3$ (250 mL). The filtrate and $CHCl_3$ washings were concentrated under reduced pressure. The resulting dark tar was dissolved in $CHCl_3$ (200 mL) and washed with 10 % aqueous $K_2CO_3$ (2 × 150 mL) and finally with brine (150 mL). The

organic layer was dried ($Na_2SO_4$), filtered, and concentrated under reduced pressure to afford a crude product which was subjected to column chromatography ($SiO_2$, hexanes/EtOAc, 4:6) to yield **3** as a yellow oil (400 mg, 20%); $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 1.66$ (m, 12H), 2.08 (m, 12H), 3.46 (t, $J = 7$ Hz, 12H), 3.62 (t, $J = 5$ Hz, 12H), 3.78 (t, $J = 5$ Hz, 12H), 3.98 (t, $J = 5$ Hz, 12H), 4.39 (t, $J = 5$ Hz, 12H), 4.95 (m, 12H), 5.77 (m, 6H), 7.87 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 28.6$, 30.1, 69.1, 69.8, 70.1, 70.6, 70.8, 107.9, 114.6, 123.8, 138.1, 148.6 ppm. HRMS (MALDI): *m/z* found: 1283.7393, calcd for $C_{72}H_{108}O_{18}Na$: 1283.7428 $[M+Na]^+$.

[**4**-$H_3$][$PF_6$]$_3$: The synthesis of this trisammonium tris(hexafluorophosphate) salt has been reported previously.[9]

[**5**-$H_3$][$PF_6$]$_3$: A mixture of 1,3,5-tris(*p*-formylphenyl)benzene (1.0 g, 2.6 mmol) and 3,5-dimethoxybenzylamine (1.3 g, 7.7 mmol) in PhMe (150 mL) was heated under reflux for 24 h and the $H_2O$ was collected in a Dean–Stark apparatus. The solution was allowed to cool down to room temperature and the solvent was evaporated under reduced pressure to give the trisimine as a yellow oil (2.1 g, 99%). This oil was dissolved in dry THF (60 mL) and dry MeOH (25 mL). After the portionwise addition of $NaBH_4$ (600 mg, 15.8 mmol), the reaction mixture was left to stir overnight. 5 M HCl (200 mL) was then added to the reaction mixture, which was concentrated to a residue that was partitioned between aqueous 2 M NaOH solution (100 mL) and $CH_2Cl_2$ (150 mL). The aqueous layer was then extracted further with $CH_2Cl_2$ (100 mL). The combined organic extracts were washed with $H_2O$ (100 mL) and then dried ($Na_2SO_4$). Filtration, followed by solvent evaporation, gave the crude product which was subjected to column chromatography ($SiO_2$, hexanes/$Et_2O$, 1:1) to afford the trisamine as a pale yellow oil (1.0 g, 46%). $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 3.84$ (s, 6H), 3.85 (s, 18H), 3.93 (s, 6H), 6.44 (t, $J = 2$ Hz, 3H), 6.60 (d, $J = 2$ Hz, 6H), 7.51 (d, $J = 8$ Hz, 6H), 7.73 (d, $J = 8$ Hz, 6H), 7.84 ppm (s, 3H). This oil was dissolved in THF/MeOH (30 mL, 25:5) and concentrated 12 M HCl (30 drops) was added. The reaction mixture was stirred for 6 h and then filtered. The resulting white solid was dissolved in hot MeOH/$H_2O$ and saturated aqueous $NH_4PF_6$ solution was added. The resulting suspension was extracted with $MeNO_2$ (50 mL). The $MeNO_2$ extract was washed with $H_2O$ (4 × 70 mL), dried ($Na_2SO_4$), filtered, and the solvent was removed under reduced pressure to give [**5**-$H_3$][$PF_6$]$_3$ as a white solid (1.2 g, 79%). $^1$H NMR (500 MHz, $CD_3CN$): $\delta = 3.79$ (s, 18H), 4.19 (s, 6H), 4.29 (s, 6H), 6.55 (t, $J = 2$ Hz, 3H), 6.62 (d, $J = 2$ Hz, 6H), 7.59 (d, $J = 8$ Hz, 6H), 7.90 (d, $J = 8$ Hz, 6H), 7.96 ppm (s, 3H); $^{13}$C NMR (125 MHz, $CD_3CN$): $\delta = 50.9$, 51.4, 55.1, 100.9, 107.7, 117.2, 125.2, 127.7, 130.1, 130.7, 132.5, 141.3, 141.4, 161.2 ppm. HRMS (ESI): *m/z* found: 844.4312, calcd for $C_{54}H_{58}O_6N_3$: 844.4320 $[M-2H-3PF_6]^+$.

[**6**-$H_3$][$PF_6$]$_3$: A solution of **3** (58 mg, 0.046 mmol) and [**5**-$H_3$][$PF_6$]$_3$ (59 mg, 0.046 mmol) in anhydrous $CH_2Cl_2$ (3.0 mL) was purged with Ar for 10 min. The catalyst [$(PCy_3)_2(Cl)_2Ru$=CHPh] (4 mg, 0.005 mmol) was added under a dry Ar atmosphere and the reaction mixture heated at 40 °C for 4 h. The solvent was evaporated off under reduced pressure and the crude product subjected to column chromatography ($SiO_2$, $CH_2Cl_2$/$MeNO_2$, 8:2) to yield [**6**-$H_3$][$PF_6$]$_3$ as a white solid (70 mg, 62%) and as a mixture of isomers. $^1$H NMR (500 MHz, $CD_2Cl_2$): $\delta = 1.77$ (m, 12H), 2.10–2.40 (m, 12H), 3.60–4.10 (m, 60H), 3.73 (s, 18H), 4.60 (m, 6H), 4.74 (m, 6H), 5.47–5.55 (m, 6H), 6.50 (m, 3H), 6.80 (m, 6H), 7.44 (m, 6H), 7.60 (m, 6H), 7.72 (br s, 3H), 7.83 (d, $J = 7$ Hz, 6H), 7.95 ppm (br s, 6H); MS (MALDI-TOF): *m/z* (%): 2313.9 $[M-PF_6]^+$ (10), 2166.5 $[M-H-2PF_6]^+$ (40), 2020.7 $[M-2H-3PF_6]^+$ (57). To complete the characterization of this mechanically interlocked "bundle", $PtO_2$ (5.4 mg) was added to a solution of [**6**-$H_3$][$PF_6$]$_3$ (48 mg, 0.020 mmol) in anhydrous THF (8 mL) and the reaction mixture was stirred under $H_2$ for 4 h. The solvent was then removed under reduced pressure and the crude product purified by column chromatography ($SiO_2$, $CH_2Cl_2$/$MeNO_2$, 8:2) to yield the fully characterized derivative of [**6**-$H_3$][$PF_6$]$_3$ as a white solid (35 mg, 72%). $^1$H NMR (500 MHz, $CD_2Cl_2$): $\delta = 1.40$–1.70 (m, 36H), 3.50–4.15 (m, 60H), 3.74 (s, 18H), 4.71 (m, 6H), 4.80 (m, 6H), 6.47 (br t, 3H), 6.79 (d, $J = 2$ Hz, 6H), 7.47 (s, 6H), 7.58 (d, $J = 8$ Hz, 6H), 7.71 (s, 3H), 7.83 (d, $J = 8$ Hz, 6H), 7.96 ppm (br s, 6H); $^{13}$C NMR (125 MHz, $CD_2Cl_2$): $\delta = 25.7$, 27.9, 29.6, 51.9, 52.8, 55.3, 67.9, 70.7, 71.2, 72.1, 73.0, 100.5, 104.4, 106.0, 120.5, 123.1, 125.8, 129.0, 129.6, 133.8, 136.5, 138.1, 145.9, 161.2 ppm; MS (MALDI): *m/z* (%): 2319.0 $[M-PF_6]^+$ (5), 2174.1 $[M-2PF_6]^+$ (40), 2028.1 $[M-H-3PF_6]^+$ (100). HRMS (ESI): *m/z* found: 1087.5990, calcd for $C_{120}H_{162}O_{24}N_3PF_6$: 1087.5606 $[M-2PF_6]^{2+}$.

**7**: A solution of **3** (96 mg, 0.076 mmol) and [**4**-$H_3$][$PF_6$]$_3$ (84 mg, 0.076 mmol) in anhydrous $CH_2Cl_2$ (3 mL) was purged with argon for 10 min. The catalyst [$(PCy_3)_2(Cl)_2Ru$=CHPh] (4 mg, 0.005 mmol) was added under a dry Ar atmosphere and the reaction mixture heated at 40 °C for 4 h. The solvent was evaporated off under reduced pressure and several drops of $Et_3N$ added, followed by $CH_2Cl_2$ (5 mL). The solvent was once again removed under reduced pressure and the crude product subjected to column chromatography ($SiO_2$, $CH_2Cl_2$/MeOH, gradient from 10:0 to 8:2) to yield **7** as a white solid (62 mg, 69%) as a mixture of isomers. $^1$H NMR (500 MHz, $CD_2Cl_2$): $\delta = 1.61$ (m, 12H), 2.02–2.17 (m, 12H), 3.47 (m, 12H), 3.51 (m, 12H), 3.76 (m, 12H), 3.97 (m, 12H), 4.37 (m, 12H), 5.31–5.40 (m, 6H), 7.88 ppm (s, 6H). HRMS (MALDI): *m/z* found: 1199.6463, calcd for $C_{66}H_{96}O_{18}Na$: 1199.6489 $[M+Na]^+$. To complete the characterization of this tris(crown ether), $PtO_2$ (5.4 mg) was added to a solution of **7** (50 mg, 0.020 mmol) in anhydrous THF (8 mL), and the reaction mixture was stirred under $H_2$ for 5 h. The solvent was then removed under reduced pressure and the crude product was subjected to column chromatography ($SiO_2$, $CH_2Cl_2$/MeOH, 95:5) to yield the *pure* fully characterized hydrogenated derivative of **7** as an off-white solid (38 mg, 75%). $^1$H NMR (500 MHz, $CD_2Cl_2$): $\delta = 1.20$–1.70 (m, 36H), 3.46 (t, $J = 6$ Hz, 12H), 3.60 (t, $J = 5$ Hz, 12H), 3.75 (t, $J = 5$ Hz, 12H), 3.97 (t, $J = 5$ Hz, 12H), 4.39 (t, $J = 5$ Hz, 12H), 7.92 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CD_2Cl_2$): $\delta = 25.5$, 28.4, 29.2, 69.7, 70.2, 70.5, 71.1, 71.2, 108.7, 124.1, 148.9 ppm; HRMS (MALDI): *m/z* found: 1205.7015, calcd for $C_{66}H_{102}O_{18}Na$: 1205.6958 $[M+Na]^+$.

"Magic ring" synthesis of [**6**-$H_3$][$PF_6$]$_3$: Catalyst [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh] (1.0 mg dissolved in $CD_2Cl_2$, 15 mol%) was added to a solution of the tris(crown ether) **7** (9.6 mg, 0.008 mmol) and the trisammonium salt [**5**-$H_3$][$PF_6$]$_3$ (10.5 mg, 0.008 mmol) in $CD_2Cl_2$ (0.5 mL) under a dry Ar atmosphere. The reaction to give [**6**-$H_3$][$PF_6$]$_3$ was followed (Figure 2) by $^1$H NMR spectroscopy at 298 K.

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