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Dynamic palladium coordination cages formed by self-assembly of extended tetra(nitrile)cavitands

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Two extended tetra(4-cyanophenylethynyl)cavitands with methylene (**6S**) and ethylene (**6L**) bridges were synthesized for coordination-driven self-assembly. Reaction with Pd(dppp)$(OTf)_2$ in a 2 : 4 ratio afforded discrete, symmetric coordination cages (**8S** and **8L**), characterized by NMR, IR and DOSY. The assemblies exhibit dynamic behavior that is dependent on concentration, with intermediate species identified through NMR titration studies. No cage formation was observed with Pt(II) or Ni(II) analogues, highlighting the importance of the kinetic lability of Pd(II) species, the size of the metal center and the geometry of the dppp ligand.

Introduction

Resorcin[4]arenes and related cavitands constitute well-established scaffolds for the design and synthesis of large-scale molecular containers.[1,2] Once a functionally tailored molecular subunit is accessible, self-assembly provides a powerful strategy for constructing increasingly complex nanoscale architectures.[3] Initially, self-assembly through hydrogen bonding was employed to link two or more cavitand-based subunits, typically bearing N–H and C=O functionalities within self-complementary motifs such as ureas, imides or carboxamides.[4–9]

Self-assembly through highly directional metal–ligand coordination bonds offers another opportunity for the preparation of nanoscale molecular containers.[10] Dalcanale and co-workers reported the synthesis and host–guest properties of coordination cages assembled from tetradentate cavitand ligands and square-planar Pd(II) and Pt(II) complexes, such as M(dppp)$(OTf)_2$ (M = Pt, Pd; dppp = 1,3-bis(diphenylphosphino) propane) (Scheme 1a).[11–15] The efficiency of the self-assembly process is governed by several factors, including: (a) the size of the chelate ring in the square-planar metal complex, (b) the intrinsic properties of the metal centre, and (c) the degree of preorganization within the cavitand scaffold.

This concept was further advanced by Kobayashi *et al.*, who demonstrated the formation of both homo- and heterocavitand cages under thermodynamic or kinetic control (Scheme 1b and c).[16–18] Hong and co-workers reported the synthesis of self-assembled nanocapsules constructed from tetra(pyridyl)cavitands and M(dppp)$(OTf)_2$ complexes (M = Pt, Pd).[19,20] Haino *et al.* prepared an octadentate cavitand bearing four bipyridyl ligands, which coordinates four silver(I) cations in a tetrahedral geometry, resulting in the self-assembly of a discrete coordination cage.[21] Additionally, hybrid supramolecular capsules were synthesized through the controlled self-assembly of two precisely designed cavitand subunits that are held together by multiple hydrogen and metal–ligand coordination bonds.[22–24]

In recent years, we have developed a novel family of enlarged cavitands, including a tetra(4-cyanophenylethynyl)cavitand designed for applications in nonlinear optics.[25–28] This compound may enable access to the missing member of the coordination cages derived from tetra(nitrile)cavitands. In view of the limited solubility of the compound in common organic solvents, we also sought to improve solubility by appending long alkyl chains to the lower rim of the cavitand scaffold. In this study, we report the coordination chemistry of two tetra(4-cyanophenylethynyl)cavitands with a series of square-planar *cis*-metal triflate complexes, including Pd(dppp)$(OTf)_2$. The enlarged lateral portals characteristic of this cavitand family may impose constraints on their efficacy as host molecules, as previously demonstrated for a related hydrogen-bonded bimolecular capsule.[29] Consequently, encapsulation studies were not pursued for these new coordination cages, as their design does not favor stable guest inclusion.

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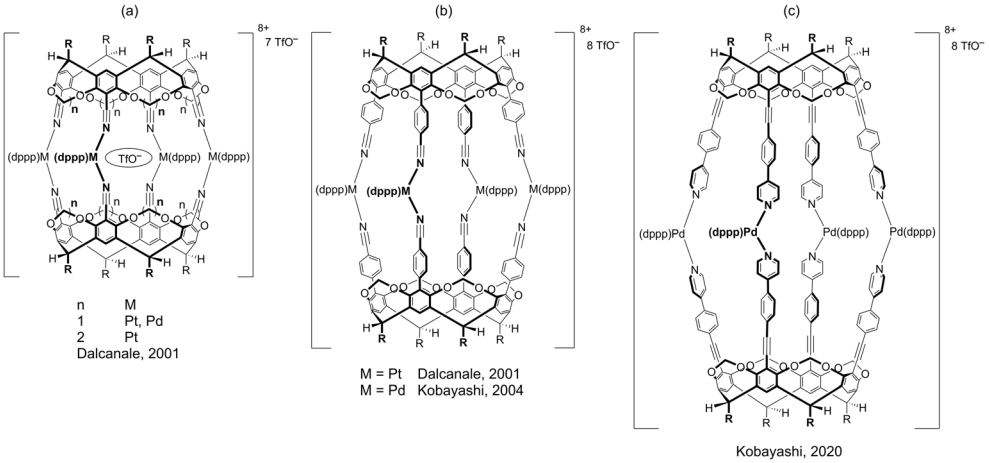
Results and discussion

Synthesis of new tetra(4-cyanophenylethynyl)cavitands

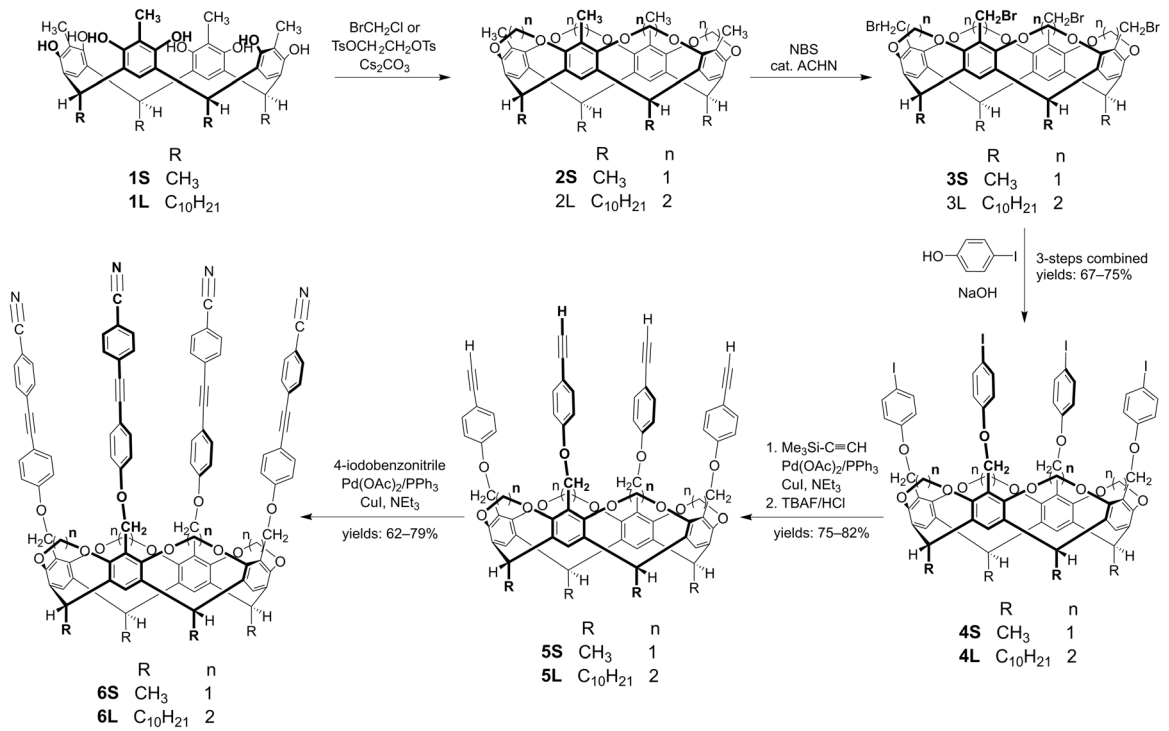
Tetra(4-cyanophenylethynyl)cavitand (**6S**), featuring methylene bridges and methyl 'feet', was synthesized following established procedures.[28] The acid-catalyzed condensation between



Scheme 1 Representative examples of coordination cages.

resorcinol and aldehyde can yield various tetrameric resorcin[4]arene isomers exhibiting different conformations (cone, boat, chair, or diamond) as well as different relative configurations of the bridging alkyl/aryl groups (*rccc*, *rcct*, *rctt*, *rtct*).[30–33] Under standard conditions, the condensation of 2-methylresorcinol with undecanal produced a mixture of isomeric macrocycles that proved inseparable by preparative chromatography. Consequently, this isomeric mixture was used directly in subsequent reactions without further purification. The major component (**1L**) was identified in the ^{1}H NMR spectrum by: (a) singlets corresponding to both aromatic and phenolic protons, and (b) a triplet associated with the bridging methine protons. This NMR pattern is consistent with a cone conformation featuring all four decyl 'feet' in axial positions (*rccc* stereoisomer). Subsequently, tetra(iodo)cavitand **4L** was synthesized from this mixture in three consecutive steps, without isolating the intermediates. Despite extensive purification efforts, these intermediates (**2L**, **3L**) remained contaminated with various isomers.

First, tetra(methyl)resorcin[4]arene **1L** was bridged using ethylene di(*p*-toluenesulfonate) to afford tetra(methyl)cavitand **2L** (Scheme 2). This intermediate was then selectively brominated with *N*-bromosuccinimide (NBS) in the presence of 1,1′-azobis(cyclohexanecarbonitrile) (ACHN) as a radical initiator to



Scheme 2 Synthesis of extended tetra(4-cyanophenylethynyl)cavitands **6S** and **6L**.

yield tetra(bromomethyl)cavitand **3L**. Subsequent reaction of **3L** with an excess of 4-iodophenol in the presence of sodium hydroxide furnished tetra(iodo)cavitand **4L**. Notably, cavitand **4L** was isolated in pure cone conformation with an overall 67% yield across the three-step sequence. Next, trimethylsilylethynyl groups were introduced at the upper rim of the cavitand scaffold under standard Sonogashira coupling conditions. Removal of the trimethylsilyl protecting groups using tetrabutylammonium fluoride trihydrate ($TBAF \cdot 3H_2O$) provided the corresponding tetra(ethynyl)cavitand **5L**. Finally, a second Sonogashira coupling of **5L** with 4-iodobenzonitrile, in the presence of $Pd(OAc)_2/PPh_3/CuI$ *in situ* catalytic system, enabled the installation of a third row of aromatic panels functionalized with nitrile groups.[34]

Cavitands **4L–6L** were fully characterized using standard techniques, including ^1H and ^{13}C NMR spectroscopy as well as ESI-MS. Notably, cavitand **6L** – featuring ethylene bridges and decyl 'feet' – exhibited broad NMR signals in CD_2Cl_2 at room temperature, attributable to rapid interconversion between two equivalent flattened C_{2v} cone conformers.[11,35] Furthermore, as anticipated, **6L** displayed significantly enhanced solubility relative to **6S**.

Coordination chemistry of the extended tetra(4-cyanophenylethynyl)cavitands 6S and 6L

New coordination compounds were obtained in 80–85% yields by reacting tetra(4-cyanophenylethynyl)cavitands **6S** or **6L** with $Pd(dppp)(OTf)_2$ in a 2 : 4 molar ratio at room temperature in CH_2Cl_2. The ^1H, ^{13}C, and ^{31}P NMR spectra of the resulting main products indicate the formation of highly symmetric species in CD_2Cl_2 (Fig. 1d and e; see also SI). In the case of the complex derived from **6L**, the ^1H NMR signals appear as very broad resonances likely due to dynamic equilibria and increased conformational flexibility of the ethylene-bridged cavitand. In contrast, the signals for the methylene-bridged cavitand **6S** remain sharp under identical conditions. Upon coordination, the ^1H signals for both cavitand scaffolds experience a slight upfield shift of approximately 0.02 ppm. A subset of aromatic protons of the Pd(dppp) fragment appear at 7.72 ppm (0.1 ppm downfield compared to uncoordinated $Pd(dppp)(OTf)_2$), while the P–CH_2 signals shift downfield by 0.14 ppm, resonating at 2.88 ppm after complexation. Because of severe spectral overlap in the aromatic region, the aromatic protons adjacent to the cyano groups could not be assigned unambiguously. In both complexes, the ^{31}P resonance was shifted upfield by approximately 3 ppm upon coordination. However, a minor signal corresponding to an unidentified side product appeared at 6.6 ppm, accounting for approximately 10% of the mixture in both cases. The triflate counterions produced a singlet at −78.5 ppm in the ^{19}F NMR spectra, indicating that all triflate anions remain outside the cavitand cavity.[11] Owing to the limited solubility of **8S** in CD_2Cl_2, detailed NMR studies, including diffusion-ordered spectroscopy (DOSY), were carried out on the more soluble analogue **8L**. Interestingly, the IR spectra revealed the presence of both uncoordinated (*ca.* 2210 cm^{-1}) and coordinated (*ca.* 2270 cm^{-1}) nitrile stretching bands for both complexes (see Fig. S17 and S23 in the SI).

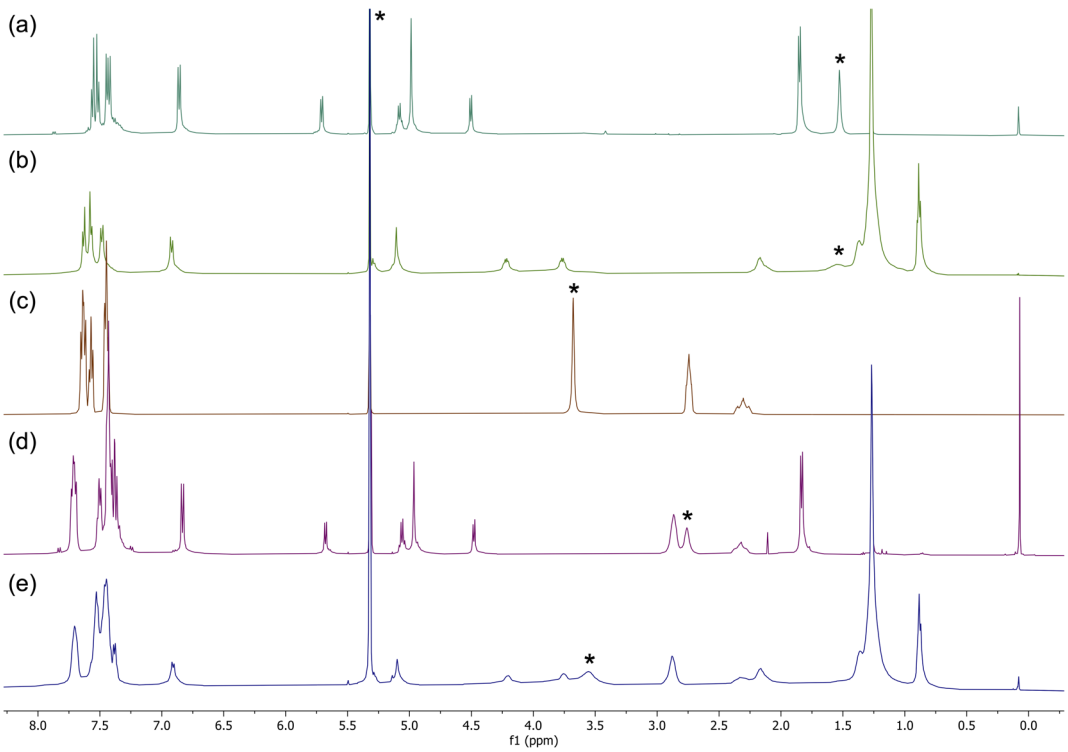
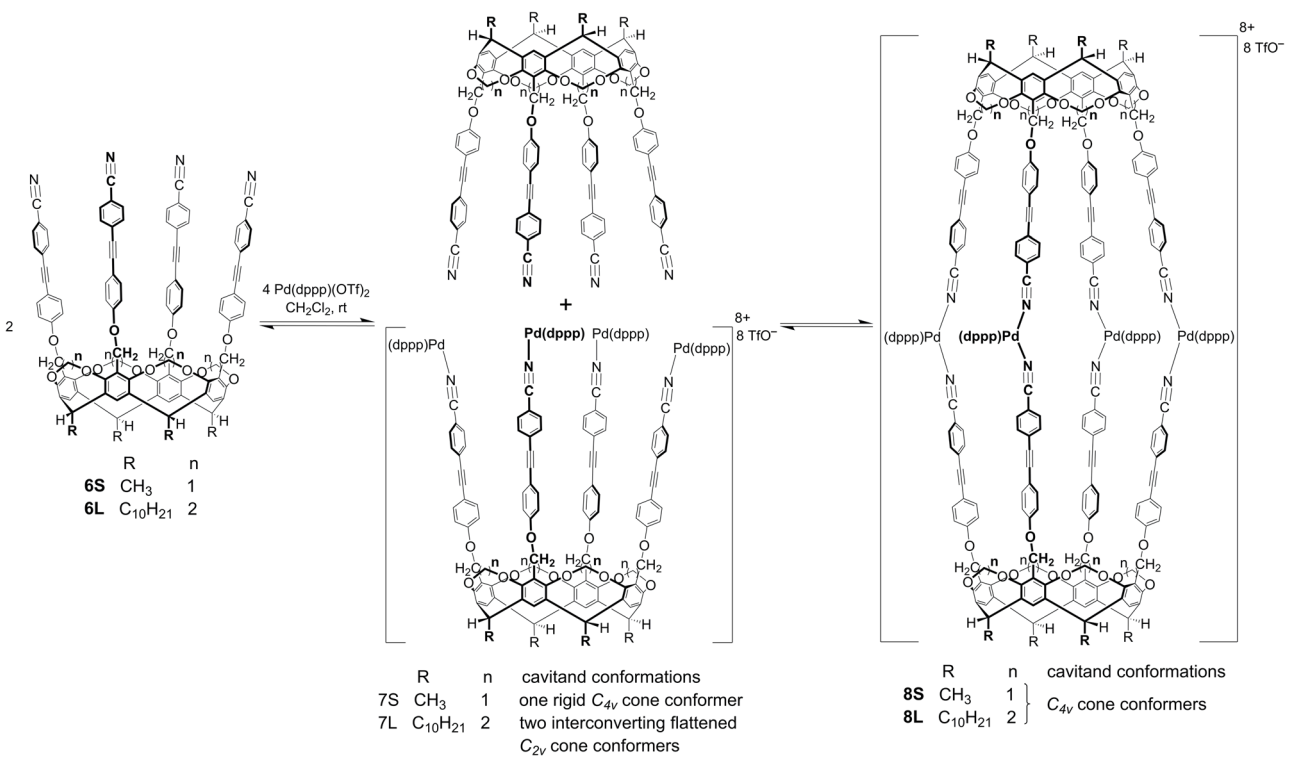


Fig. 1 ^1H NMR spectra (500 MHz, CD_2Cl_2) of (a) **6S**; (b) **6L**; (c) $Pd(dppp)(OTf)_2$; (d) **8S** and (e) **8L**. Asterisks (*) indicate residual CD_2Cl_2 and minor impurities, including water.

Variable-temperature ^{1}H NMR spectra of compound **8L** were recorded between 238 K and 388 K in $CDCl_2$–$CDCl_2$ (Fig. S19 in the SI). Upon increasing the temperature, the signals shifted gradually downfield, the broad resonances partially sharpened and began to display fine structure, consistent with an increased exchange rate between closely related sub-conformations of compound **8L**. Unfortunately, the compound decomposed above 388 K before reaching fast-exchange conditions for all resonances. At lower temperatures, the resonances broadened even further, and coalescence was observed for several resonances (*e.g.* at 3.8 and 4.2 ppm). However, the signals did not resolve into sharp peaks in the slow-exchange regime even at 238 K; further cooling was prevented by freezing of the solvent.

The DOSY experiments were carefully set up to ensure a negligible temperature gradient, thereby providing reliable diffusion coefficients (see Experimental). In **8L**, the signals arising from both the cavitand skeleton and the Pd(dppp) moieties diffuse together as a single molecular entity. DOSY measurements in $CDCl_2$–$CDCl_2$ (3.4 mM, 298 K) yielded average diffusion coefficients of 8.06×10^{-11} m^2 s^{-1} (range: 7.55 to 8.71 $\times 10^{-11}$ m^2 s^{-1}) for the free tetradentate ligand **6L** and 6.45×10^{-11} m^2 s^{-1} (range: 6.15 to 6.74 $\times 10^{-11}$ m^2 s^{-1}) for the coordination complex **8L**, respectively (Fig. S11 and S21 in the SI). The observed decrease in diffusion coefficient upon complexation reflects the formation of a larger, more slowly diffusing entity. The magnitude of this change is consistent with reported values for similar cavitand-based monomer/dimer systems.[21,29,36,37] Derived from the Stokes–Einstein equation, the cubed ratio of the two diffusion coefficients corresponds to the inverse ratio of their molar volumes.[38] On this basis, the volume of complex **8L** was calculated to be 1.95 times that of **6L**. These results rule out intramolecular complexation, where coordination would involve two adjacent nitrile groups on the same cavitand, and instead support the formation of an intermolecularly bridged self-assembly.

NMR titration experiments were performed to investigate the formation of the coordination complex derived from cavitand **6L**. Upon addition of 0.5 equiv. of Pd(dppp)$(OTf)_2$ to a 3 mM CD_2Cl_2 solution of **6L**, diagnostic downfield ^{1}H and upfield ^{31}P NMR signals emerged, indicating complex formation (Fig. S24 and S25 in the SI). Further stepwise additions of the Pd precursor (up to 4 equiv.) led to gradual upfield shifts of the characteristic proton resonances, while the ^{31}P signal shifted downfield. For comparison, mono- and bis-benzonitrile coordination complexes were also synthesized as reference compounds. The ^{31}P NMR signal of Pd(dppp)(PhC≡N)$(OTf)_2$ appears at 15.5 ppm in CD_2Cl_2, closely matching the resonance observed at a **6L**/[Pd] molar ratio of 2 : 8. Similarly, the ^{31}P resonance of Pd(dppp)$(PhC{\equiv}N)_2(OTf)_2$ is found at 14.5 ppm in CD_2Cl_2, nearly identical to the signal observed at a **6L**/[Pd] ratio of 2 : 4 and corresponding to the resonance of the isolated coordination complex **8L**. This behavior contrasts with that of smaller coordination cages, where the cage was the sole product regardless of the stoichiometric excess of either component (Scheme 1a).[11] Furthermore, the formation of the cage complex **8L** from the reaction of **6L** with Pd(dppp)$(OTf)_2$ in a 2 : 4 molar ratio exhibits concentration dependence: the equilibrium shifts toward cage formation at higher concentrations (Fig. S26 in the SI).



Scheme 3 Dynamic behavior of the cavitand-based palladium coordination cages 8S and 8L.

Together, these findings support the conclusion that cavitand **6L** and Pd(dppp)$(OTf)_2$ self-assemble at a 2 : 4 molar ratio to form coordination cage **8L** in CD_2Cl_2 and in $CDCl_2$–$CDCl_2$ (Scheme 3). Formation of this highly symmetric D_{4h} cage structure requires that the tetra(4-cyanophenylethynyl)cavitand subunits adopt a C_{4v} symmetry cone conformer, in which all four nitriles have the same angle with respect to the C_4 symmetry axis.[11] NMR titration experiments indicate a dynamic equilibrium between free cavitand **6L**, coordination cage **8L**, and an intermediate species **7L**, in which only one nitrile group coordinates to the palladium center. The intermediate is presumed to exist in a state of rapid equilibrium between two equivalent C_{2v} flattened cone conformers. The pronounced line broadening observed in the NMR spectra suggests rapid exchange between all these species on the NMR timescale. In contrast, the faster temporal resolution of IR spectroscopy enables differentiation between uncoordinated (*ca.* 2210 cm^{-1}) and coordinated nitrile groups (*ca.* 2270 cm^{-1}). Moreover, the absence of detectable peaks for either **8S** or **8L** by MALDI and ESI-TOF mass spectrometry suggests that the nitrile–palladium coordination bonds are comparatively weak and dynamic in nature when contrasted with earlier coordination cages.[11–13,16,17]

Attempts to form coordination cages by reacting tetra(4-cyanophenylethynyl)cavitands **6S** or **6L** with other square-planar *cis*-metal triflate complexes – such as Pd(dppe)$(OTf)_2$ (dppe = 1,2-bis(diphenylphosphino)ethane), Pt(dppp)$(OTf)_2$, *cis*-Pt$(PEt_3)_2(OTf)_2$, Ni(dppe)$(OTf)_2$, Ni(dppp)$(OTf)_2$ and Ni(dppf)$(OTf)_2$ (dppf = 1,1′-bis(diphenylphosphino)ferrocene) – were unsuccessful. In the case of the nickel-based complexes, the tetranitrile ligands were recovered unreacted, suggesting no significant coordination occurred. Reactions involving the platinum complexes resulted in the formation of multiple unidentified species, indicating non-selective or uncontrolled coordination. When these reactions were carried out at elevated temperature (85 °C) in tetrachloroethane, insoluble materials precipitated from the reaction mixtures, consistent with the formation of oligomeric or polymeric species rather than discrete cages.

Both the size of the chelate ring and the nature of the metal center exert a significant influence on cage formation. In good agreement with previous findings,[11] successful self-assembly into a cage structure was observed only with dppp, whose P–M–P bite angle (approximately 90°) closely matches the ideal geometry for square-planar coordination. The same study found that self-assembly of the ethylene-bridged tetra(nitrile)cavitands proceeds only with Pt(dppp)$(OTf)_2$, as the Pd(II) analogues proved ineffective under the same conditions (Scheme 1a). In contrast, on the enlarged cavitand platform presented here, the desired cage could not be obtained using the Pt(dppp)$(OTf)_2$ precursor, either under standard conditions or at elevated temperatures. This limitation can be attributed to the greater kinetic inertness of platinum compared to palladium, which may hinder the reversibility and dynamic 'error–correction processes' necessary for thermodynamically controlled self-assembly. Furthermore, the complete lack of reactivity observed with the nickel complexes is likely due to the inherently weak coordination between nitrile groups and nickel(II), preventing effective complex formation.

Conclusions

In this study, we synthesized two extended tetra(4-cyanophenylethynyl)cavitands, **6S** and **6L**, featuring rigid methylene and more flexible ethylene bridging units, respectively. Their stepwise functionalization enabled the installation of terminal nitrile groups suitable for coordination-driven self-assembly. Coordination experiments with Pd(dppp)$(OTf)_2$ in a 2 : 4 molar ratio led to the formation of discrete, symmetric coordination cages (**8S** and **8L**), as evidenced by NMR spectroscopy, DOSY measurements and IR analysis. The assembly process is dynamic and reversible, with NMR titration studies revealing the presence of intermediates and a concentration-dependent equilibrium between the free ligand and the final cage structure. Notably, cage formation was not observed with Pt(II) or Ni(II) analogues, emphasizing the essential role of both the geometric compatibility of the dppp ligand and the kinetic lability of the Pd(II) metal center. These findings may further advance the design of cavitand-based coordination architectures and highlight the utility of nitrile–metal interactions in dynamic supramolecular assemblies.

Experimental

General experimental methods

All reagents and organometallic precursors were purchased from Merck and used without further purifications. Square-planar *cis*-metal triflate complexes (ref. 11) and cavitands **1S**–**6S** (ref. 25–28) were synthesized according to literature procedures; their NMR spectra were identical to those previously reported. ^1H, ^{31}P and ^{13}C NMR spectra were recorded at 500, 202 and 125 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) downfield from the solvent residual peaks: $CDCl_3$ (7.27 ppm for ^1H, 77.0 ppm for ^{13}C), CD_2Cl_2 (5.32 ppm for ^1H, 53.84 ppm for ^{13}C) and DMSO-d_6 (2.50 ppm for ^1H, 39.51 ppm for ^{13}C). High-resolution mass spectra were obtained using ESI-TOF technique on a Bruker maXis 4G mass spectrometer.

Self-diffusion measurements were performed with the bipolar gradient pulse sequence[39] using a Bruker Avance III NMR spectrometer operating at 600 MHz proton frequency. The instrument was equipped with a 5 mm broadband direct observe BBFO probe with a shielded *z*-gradient coil and a GAB gradient amplifier (10 A, maximum gradient strength 52.5 G cm^{-1}). The diffusion experiments were performed at 298 K and the gradient strength was calibrated using a Shigemi tube filled with H_2O to a height of 4.0 mm and imaging this water cylinder.[40] The diffusion experiments were performed by varying the gradient strength between 5% and 95% of the maximum strength in 16 single experiments using an acquisition time of 2 s and 16 scans, while keeping the diffusion times and gradient lengths constant. The diffusion time was set to 90 ms (big delta), and a gradient duration of 1.5 ms was applied (little delta). The intensity decrease of the signal of interest was determined and fitted with a Bruker t1/t2 software package suitable for DOSY experiments, which is included in the Topspin 3.6 software package.[41] Variable temperature

experiments of **8L** in $CDCl_2$–$CDCl_2$ were performed in the range of 238 to 388 K on a broadband inverse detection probe (BBI) equipped with a shielded *z*-gradient. The temperature was calibrated using a methanol standard for low and a glycerol sample for high temperatures, showing accuracy within ±0.2 K.

Synthetic procedures

Tetra(methyl)resorcin[4]arene (1L). 2-Methylresorcinol (10.0 g, 80.55 mmol) was dissolved in a mixture of ethanol (60 mL) and 37% aqueous HCl (18 mL). The reaction mixture was cooled to 0 °C before undecanal (16.6 mL, 80.55 mmol) was added dropwise over 15 minutes. After the addition was complete, the solution was allowed to warm to rt and heated to reflux at 80 °C for 16 hours. Upon completion, the reaction was cooled to rt, the precipitate was collected by filtration and washed with a cold 1 : 1 ethanol/water mixture until the washings were neutral (pH ≈ 7). The crude solid was triturated with hot methanol (100 mL) and dried under reduced pressure to yield the title compound **1L** as a peach-colored solid (18.5 g, 83%). Mp 230–235 °C. ν_{max}(KBr): 1098, 1165, 1263, 1337, 1441, 1477, 1612, 2853, 2924, 3389 cm^{-1}. Major isomer: ^1H NMR (500 MHz, DMSO-d_6) δ 0.85 (12H, t, $J = 7.0$ Hz, CH_3), 1.10–1.36 (64H, m, $(CH_2)_8$), 1.94 (12H, s, $ArCH_3$), 2.17 (8H, m, CH_2CH), 4.18 (4H, m, CHCH_2), 7.19 (4H, s, ArH), 8.64 (8H, s, OH). $^{13}C\{^1H\}$ NMR (500 MHz, DMSO-d_6) δ 10.0 (CH_3), 13.8 ($ArCH_3$), 22.2 (CH_2), 28.0 (CH_2), 28.9 (CH_2), 29.1 (CH_2), 29.29 (CH_2), 29.31 (CH_2), 29.4 (CH_2), 31.4 (CH_2), 33.5 (*C*HCH_2), 34.2 (*C*H_2CH), 111.6 (Ar), 120.1 (Ar), 124.3 (Ar), 149.2 (Ar). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{72}H_{113}O_8$ 1105.8430; found: 1105.8453.

Tetra(iodo)cavitand (4L). Tetra(methyl)resorcin[4]arene **1L** (6.00 g, 5.43 mmol) and cesium carbonate (14.25 g, 43.73 mmol) were stirred under an argon atmosphere in dry DMF (120 mL) for 30 minutes. Ethylene di(*p*-toluenesulfonate) (16.20 g, 43.73 mmol) was then added to the reaction mixture. The resulting suspension was stirred at 100 °C for 3 days. After cooling to rt, the solvent was removed under reduced pressure. The residue was treated with water (150 mL) and CH_2Cl_2 (150 mL), and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with water (2 × 200 mL), dried over anhydrous $MgSO_4$ and concentrated under vacuum to yield intermediate **2L** as a brown, viscous oil. This crude product was used directly in the next step without further purification. Major component: ^1H NMR ($CDCl_3$, 500 MHz): δ 0.88 (12H, t, $J = 7.0$ Hz, CH_3), 1.15–1.39 (64H, m, $(CH_2)_8$), 2.05 (8H, m, CH_2CH), 2.18 (12H, s, $ArCH_3$), 3.50 (8H, m, inner of OCH_2CH_2O), 4.27 (8H, m, outer of OCH_2CH_2O), 5.20 (4H, t, $J =$ 8.1 Hz, CHCH_2), 7.21 (4H, s, Ar).

Tetra(methyl)cavitand **2L** was dissolved in benzene (200 mL) and added to *N*-bromosuccinimide (15.60 g, 87.46 mmol) and 1,1′-azobis(cyclohexanecarbonitrile) (1.34 g, 5.47 mmol) under an argon atmosphere. The reaction mixture was stirred at 80 °C for 2 days. After cooling to rt, the upper liquid layer was removed by decantation, and the solvent was evaporated under reduced pressure. The residue was dissolved in $CHCl_3$ (200 mL) and washed with 1 M NaOH (3 × 200 mL). The combined aqueous layers were extracted with another portion of $CHCl_3$ (50 mL). The combined organic phases were washed with water (100 mL), dried over anhydrous $MgSO_4$ and concentrated under vacuum to afford intermediate **3L** as a brown, viscous oil. This material was used in the subsequent step without further purification. Major component: ^1H NMR ($CDCl_3$, 500 MHz): δ 0.88 (12H, t, $J = 7.0$ Hz, CH_3), 1.15–1.39 (64H, m, $(CH_2)_8$), 2.05 (8H, m, CH_2CH), 4.17 (8H, m, inner of OCH_2CH_2O), 4.63 (8H, m, outer of OCH_2CH_2O), 4.76 (8H, s, $ArCH_2Br$), 5.20 (4H, t, $J =$ 8.1 Hz, CHCH_2), 7.43 (4H, s, Ar).

To a solution of 4-iodophenol (12.10 g, 54.66 mmol) in THF (50 mL) was added aqueous NaOH (1.825 M, 30 mL), and the mixture was stirred at rt for 30 minutes. This solution was then added dropwise to a solution of tetra(bromomethyl)cavitand **3L** in THF (100 mL). The resulting mixture was refluxed at 70 °C for 16 hours, then cooled to rt. The reaction mixture was washed with 1 M NaOH (100 mL) and $CHCl_3$ (100 mL). The organic layer was further washed with 1 M NaOH (2 × 100 mL), and the combined aqueous layers were extracted with another portion of $CHCl_3$ (50 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting residue was triturated with methanol (60 mL), and the solid that precipitated was collected and dried *in vacuo* to afford the title compound **4L** as a yellow solid (7.60 g, combined yield: 67%). Mp 103–105 °C. ν_{max}(KBr): 818, 995, 1061, 1096, 1234, 1466, 1485, 1584, 2853, 2924 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 0.89 (12H, t, $J = 7.0$ Hz, CH_3), 1.18–1.43 (64H, m, $(CH_2)_8$), 2.14 (8H, m, CH_2CH), 3.75 (8H, m, inner of OCH_2-CH_2O), 4.21 (8H, m, outer of OCH_2CH_2O), 5.04 (8H, s, $ArCH_2O$), 5.30 (4H, t, $J = 8.0$ Hz, CHCH_2), 6.66 (8H, d, $J = 9.0$ Hz, Ar), 7.50 (4H, s, Ar), 7.57 (8H, d, $J = 9.0$ Hz, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 14.2 (CH_3), 22.7 (CH_2), 27.9 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.68 (CH_2), 29.69 (CH_2), 29.72 (CH_2), 31.9 (CH_2), 33.9 (*C*HCH_2), 34.4 (*C*H_2CH), 61.1 ($ArCH_2O$), 73.5 (OCH_2CH_2O), 83.3 (Ar), 116.8 (Ar), 123.6 (Ar), 125.3 (Ar), 135.9 (Ar), 138.5 (Ar), 153.8 (Ar), 158.0 (Ar). HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{104}H_{132}O_{12}I_4Na$ 2103.5790; found: 2103.5776.

Tetra(ethynyl)cavitand (5L). Tetra(iodo)cavitand **4L** (4.5 g, 2.162 mmol), $Pd(OAc)_2$ (33.0 mg, 0.147 mmol), PPh_3 (80 mg, 0.305 mmol), and CuI (206 mg, 1.081 mmol) were placed under an argon atmosphere in a Schlenk tube and dissolved in dry THF (100 mL). Trimethylsilylacetylene (1.35 mL, 9.513 mmol) and triethylamine (4.84 mL, 34.6 mmol) were added to the reaction mixture, which was then stirred at 65 °C for 16 hours. After cooling to room temperature, the reaction mixture was filtered to remove insoluble materials. The solvent was removed under reduced pressure, and the residue was treated with MeOH (40 mL). The resulting precipitate was collected by filtration and dried *in vacuo* to yield tetra(trimethylsilylethynyl) cavitand intermediate as a solid. ^1H NMR ($CDCl_3$, 500 MHz): δ 0.23 (36H, s, $Si(CH_3)_3$), 0.89 (12H, t, $J = 7.1$ Hz, CH_3), 1.18–1.42 (64H, m, $(CH_2)_8$), 2.14 (8H, m, CH_2CH), 3.75 (8H, m, inner of OCH_2CH_2O), 4.20 (8H, m, outer of OCH_2CH_2O), 5.07 (8H, s, $ArCH_2O$), 5.30 (4H, t, $J = 8.1$ Hz, CHCH_2), 6.79 (8H, d, $J = 8.9$ Hz, Ar), 7.40 (8H, d, $J = 8.9$ Hz, Ar), 7.50 (4H, s, Ar).

To a solution of the tetra(trimethylsilylethynyl)cavitand intermediate in THF (80 mL) was added tetrabutylammonium fluoride trihydrate (3.14 g, 9.944 mmol). The reaction mixture

was stirred at rt for 30 minutes. The solvent was then removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 (60 mL). This solution was washed sequentially with 10% aqueous HCl (60 mL) and water (2 × 100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was triturated with methanol (30 mL), the resulting solid was collected and dried *in vacuo* to afford the title compound **5L** as a brown solid (2.7 g, 75%). Mp 100–103 °C. ν_{max}(KBr): 831, 997, 1063, 1096, 1169, 1238, 1287, 1466, 1506, 1605, 2106, 2853, 2924, 3287 cm^{-1}.^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.90 (12H, t, J = 7.1 Hz, CH_3), 1.20–1.43 (64H, m, $(CH_2)_8$), 2.15 (8H, m, CH_2CH), 3.00 (4H, s, C≡CH), 3.77 (8H, m, inner of OCH_2CH_2O), 4.23 (8H, m, outer of OCH_2CH_2O), 5.09 (8H, s, $ArCH_2O$), 5.32 (4H, t, J = 8.1 Hz, CHCH$_2$), 6.83 (8H, d, J = 8.9 Hz, Ar), 7.43 (8H, d, J = 8.9 Hz, Ar), 7.52 (4H, s, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 14.1 (CH_3), 22.7 (CH_2), 27.9 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.63 (CH_2), 29.69 (CH_2), 29.73 (CH_2), 31.9 (CH_2), 34.0 (*C*HCH$_2$), 34.5 (*C*H$_2$CH), 61.1 ($ArCH_2O$), 73.5 (OCH_2CH_2O), 76.1 (C≡C), 83.3 (C≡C), 114.4 (Ar), 114.9 (Ar), 123.6 (Ar), 125.3 (Ar), 133.8 (Ar), 135.9 (Ar), 153.9 (Ar), 158.5 (Ar). HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{112}H_{136}O_{12}Na$ 1695.9924; found: 1695.9917.

Tetra(4-cyanophenylethynyl)cavitand (6L). Tetra(ethynyl) cavitand **5L** (500 mg, 0.30 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PPh_3 (13.1 mg, 0.050 mmol), CuI (29 mg, 0.15 mmol) and 4-iodobenzonitrile (275 mg, 1.20 mmol) were placed under an argon atmosphere in a Schlenk tube and dissolved in dry THF (20 mL). Triethylamine (0.672 mL, 4.8 mmol) was then added, and the reaction mixture was stirred at 65 °C for 16 hours. After cooling to rt, the mixture was filtered to remove insoluble materials, and the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (50 mL) and washed with water (2 × 50 mL). The combined aqueous layers were extracted with another portion of CH_2Cl_2 (30 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The title compound **6L** was obtained as a light brown solid (387 mg, 62%) after reprecipitation from CH_2Cl_2/MeOH and drying under vacuum. Mp 140–142 °C. ν_{max}(KBr): 835, 993, 1061, 1096, 1134, 1238, 1466, 1512, 1599, 2214 (C≡N), 2853, 2924 cm^{-1}.^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.90 (12H, t, J = 7.1 Hz, CH_3), 1.15–1.45 (64H, m, $(CH_2)_8$), 2.16 (8H, m, CH_2CH), 3.79 (8H, m, inner of OCH_2CH_2O), 4.25 (8H, m, outer of OCH_2CH_2O), 5.13 (8H, s, $ArCH_2O$), 5.33 (4H, t, J = 8.0 Hz, CHCH$_2$), 6.90 (8H, d, J = 8.8 Hz, Ar), 7.49 (8H, d, J = 8.8 Hz, Ar), 7.52–7.64 (20H, m, Ar). ^{1}H NMR (CD_2Cl_2, 500 MHz): δ 0.89 (12H, t, J = 7.0 Hz, CH_3), 1.10–1.42 (64H, m, $(CH_2)_8$), 2.17 (8H, m, CH_2CH), 3.76 (8H, m, inner of OCH_2CH_2O), 4.22 (8H, m, outer of OCH_2CH_2O), 5.11 (8H, s, $ArCH_2O$), 5.30 (4H, t, J = 7.9 Hz, CHCH$_2$), 6.92 (8H, d, J = 8.6 Hz, Ar), 7.48 (8H, d, J = 8.6 Hz, Ar), 7.52–7.66 (20H, m, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 14.1 (CH_3), 22.7 (CH_2), 27.9 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.69 (CH_2), 29.70 (CH_2), 29.72 (CH_2), 31.9 (CH_2), 34.0 (*C*HCH$_2$), 34.4 (*C*H$_2$CH), 61.3 ($ArCH_2O$), 73.5 (OCH_2CH_2O), 87.0 (C≡C), 93.6 (C≡C), 111.2, 114.7, 114.9, 118.5, 123.4, 125.5, 128.4, 131.8, 132.0, 133.5, 136.0, 153.9, 158.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{140}H_{148}N_4O_{12}Na$ 2100.0986; found: 2100.0987.

Coordination cage 8S. Tetra(4-cyanophenylethynyl)cavitand **6S** (100 mg, 0.066 mmol) was suspended in dry CH_2Cl_2 (15 mL) under an argon atmosphere. Pd(dppp)$(OTf)_2$ (108 mg, 0.132 mmol) was added, and the mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure to afford the product as a brown, microcrystalline solid (177 mg, 85% yield). ν_{max}(KBr): 511, 638, 668, 837, 973, 1030, 1248, 1283, 1513, 1597, 2214 (free C≡N), 2268 (coordinated C≡N), 2943 cm^{-1}.^{1}H NMR (CD_2Cl_2, 500 MHz): δ 1.85 (24H, d, J = 7.4 Hz, CH_3CH), 2.33 (8H, br m, $PCH_2CH_2CH_2P$), 2.88 (16H, br s, $PCH_2CH_2CH_2P$), 4.49 (8H, d, J = 7.3 Hz, inner of OCH_2O), 4.98 (16H, s, $ArCH_2O$), 5.07 (8H, q, J = 7.4 Hz, CHCH$_3$), 5.69 (8H, d, J = 7.3 Hz, outer of OCH_2O), 6.85 (16H, d, J = 8.8 Hz, Ar), 7.30–7.55 (104H, m, Ar), 7.72 (32H, m, Ar). ^{13}C{^{1}H} NMR (CD_2Cl_2, 125 MHz): δ 16.3 (*C*H$_3$CH), 18.8 ($PCH_2CH_2CH_2P$), 22.5 (d, $J_{(C-P)}$ = 45 Hz, $PCH_2CH_2CH_2P$), 31.8 (*C*HCH$_3$), 61.2 ($ArCH_2O$), 87.3 (C≡C), 95.2 (C≡C), 100.5 (OCH_2O), 108.7, 114.9, 115.2, 120.9, 121.0 (q, $J_{(C-F)}$ = 320 Hz), 121.9, 122.9, 124.6, 125.1, 130.1 (m), 132.1, 133.3, 133.4, 133.8 (m), 133.9, 139.4, 154.4, 159.9. ^{31}P NMR (CD_2Cl_2, 202 MHz): δ 14.2 (s). ^{19}F NMR (CD_2Cl_2, 564 MHz): δ −78.6 (s).

Coordination cage 8L. Tetra(4-cyanophenylethynyl)cavitand **6L** (100 mg, 0.048 mmol) was dissolved in dry CH_2Cl_2 (15 mL) under an argon atmosphere. Pd(dppp)$(OTf)_2$ (78.4 mg, 0.096 mmol) was added, and the reaction mixture was stirred at room temperature for 1 hour. The solvent was removed under reduced pressure to yield the product as a brown, microcrystalline solid (143 mg, 80%). ν_{max}(KBr): 511, 638, 692, 837, 1030, 1099, 1170, 1244, 1283, 1466, 1513, 1597, 1636, 2211 (free C≡N), 2273 (coordinated C≡N), 2853, 2924 cm^{-1}. ^{1}H NMR (CD_2Cl_2, 500 MHz): δ 0.88 (24H, br t, J = 7.0 Hz, CH_3), 1.10–1.42 (128H, br m, $(CH_2)_8$), 2.16 (16H, br m, CH_2CH), 2.32 (8H, br m, $PCH_2CH_2CH_2P$), 2.88 (16H, br s, $PCH_2CH_2CH_2P$), 3.76 (16H, br m, inner of OCH_2CH_2O), 4.20 (16H, br m, outer of OCH_2CH_2O), 5.10 (16H, br s, $ArCH_2O$), 5.29 (8H, br m, CHCH$_2$), 6.91 (16H, br d, J = 8.5 Hz, Ar), 7.34–7.60 (104H, br m, Ar), 7.71 (32H, br s, Ar). ^{13}C{^{1}H} NMR (CD_2Cl_2, 125 MHz): δ 14.3 (CH_3), 18.7 (PCH_2-*C*H$_2$CH$_2$P), 22.7 (d, $J_{(C-P)}$ = 40 Hz, $PCH_2CH_2CH_2P$), 23.1, 28.4, 29.8, 30.1 (double intensity, CH_2), 30.2 (double intensity, CH_2), 32.4, 34.5 (*C*HCH$_2$), 35.0 (*C*H$_2$CH), 61.7 ($ArCH_2O$), 73.9 (OCH_2-CH_2O), 87.3 (C≡C), 95.3 (C≡C), 108.9, 115.0, 115.4, 124.0, 124.6, 125.0, 128.2, 128.7, 129.7, 130.1, 132.1, 132.8, 133.3, 133.8, 136.4, 154.4, 159.7. ^{31}P NMR (CD_2Cl_2, 202 MHz): δ 14.5 (br s). ^{19}F NMR (CD_2Cl_2, 564 MHz): δ −78.5 (s).

Conflicts of interest

The authors declare no conflicts of interest.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: NMR and IR spectra of the synthesized compounds, along with additional experimental details. See DOI: https://doi.org/10.1039/d6ra00433d.

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