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Chiral M_3L_2 Self-Assembled Capsules through Metal Coordination of Enantiopure Ligating Benzocyclotrimers: NMR Spectroscopic and ESI Mass Spectrometric Investigation

Stefano Tartaggia,[a] Ottorino De Lucchi,[a] Andrea Gambaro,[b] Roberta Zangrando,[b] Fabrizio Fabris,*[a] and Alessandro Scarso*[a]

Abstract: The synthesis of enantiopure (+)-benzotricamphor *syn*-**5**, an important chiral C_3-symmetric rigid building block for supramolecular applications, was studied in detail to reduce the number of steps and to increase the diastereoselectivity and overall yield. The new synthetic procedure allowed larger amounts of *syn*-**5** to be obtained and used for the preparation of new derivatives, such as the corresponding *tris*-trifluoromethanesulfonate *syn*-**12**, which was efficiently transformed into (+)-benzotribornenetrinitrile *syn*-**1** and (+)-benzotribornenetris(ethynyl-4-pyridine) *syn*-**2**. The previously reported (+)-benzotricamphortrioxime *syn*-**6** was transformed into tris-nitrile *syn*-**3** by Beckman reaction. Compounds *syn*-**1**–**3** were employed as multidentate ligands for silver(I) and platinum(II) centres in apolar solvents. The linear coordination geometry of Ag^I and square-planar geometry of *cis*-chelated Pt^{II} in combination with the chiral tripodal ligands *syn*-**1**–**3** led to the formation of chiral enantiopure capsules with M_3L_2 stoichiometry, as confirmed by 2D NMR NOESY and DOSY experiments as well as ESI mass spectrometry.

Keywords: cyclotrimerization · Heck reaction · platinum · self-assembly · silver

Introduction

Compared to hydrogen bonding, metal–ligand coordination is characterized by high binding enthalpies, and this property can be exploited for the construction of stable supramolecular aggregates both in organic solvents and in water.[1] The large number of possible combinations of metal cations and coordinating functional groups inspired the development of a variety of nanometric supramolecules characterized by the most diverse shapes and geometries.[2] Obtaining definite aggregates requires the proper combination of preferred coordination of the metal centre and the topology of the polydentate ligand in terms of geometry, shape and binding constant. In particular, rigid concave and symmetrical ligands endowed with preoriented coordinating residues favour the self-assembly of well-defined structures rather than unspecific oligomeric or polymeric aggregates. The inner cavities of these well-defined aggregates enable host–guest interactions with appropriate molecular species, displaying a high degree of selectivity at all levels. Vase-like[3] and capsule-like[4] host structures are both possible. In particular, metal-coordinated self-assembled hosts have been employed as nanometric reaction chambers for the stabilization of reactive species and weak assemblies[5] or isolated hydrogen-bonding pairs.[6] An important application of metal-based capsules is their use as supramolecular catalysts for selective transformations[7] with saturation kinetics, competitive binding and turnover ability, all of which are typical features of enzymes.

Chiral metal–ligand-based capsules can be obtained by use of achiral ligands that arrange around an octahedral metal centre in Δ or Λ enantiomeric configuration leading to racemic capsules that can be resolved in some cases by inclusion of an enantiopure guest.[8] An alternative approach for the preparation of chiral capsules is based on the use of enantiomerically pure ligands coordinated to metals.[9] This strategy was exploited for the preparation of a chiral enantiopure square bipyramidal capsule acting as a catalyst to induce asymmetry in a 2+2 cycloaddition.

Herein we present the synthesis and characterization of supramolecular dimeric capsules held together by metal–ligand coordination between tripodal enantiopure tris-nitrile (*syn*-**1**, *syn*-**2**) and tris-pyridine (*syn*-**3**) ligands sharing a benzocyclotrimeric rigid scaffold and Ag^I or Pt^{II} centres.

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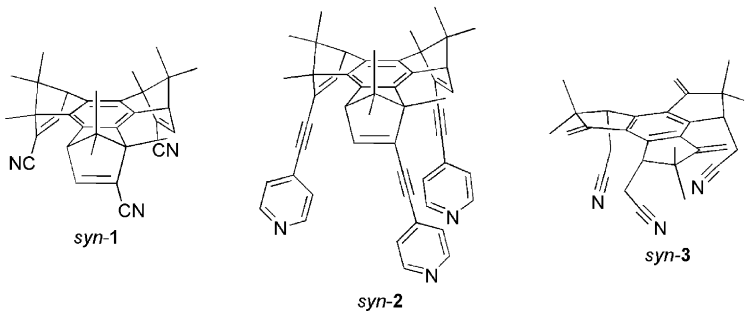
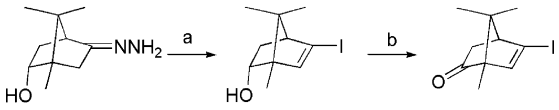


syn-1 *syn*-2 *syn*-3

Results and Discussion

Synthesis of tripodal ligands: Benzocyclotrimers[10] are peculiar, rigid, cup-shaped and functionalized molecules that have been employed for different purposes, such as the preparation of sumanene, the smallest fragment of fullerene[11] and its enantiopure trimethyl derivative.[12] Recently, benzocyclotrimers have also found applications in supramolecular chemistry, by furnishing appropriate scaffolds for the preparation of pH-sensitive molecular baskets[13] and receptors for C_{60}.[14] Enantiopure (+)-benzotriborneol *syn*-**4** discriminates chiral ammonium ions[15] and has high affinity to water.[16] The diverse reactivity of the carbonyl group in enantiopure cyclotrimers is extremely appealing for applications in supramolecular chemistry, as demonstrated in the case of (+)-benzotricamphor *syn*-**5**, which was conveniently employed for the synthesis of (+)-benzotricamphor trisoxime *syn*-**6**, which self-assembles into a dimeric unit with a cavity suitable for hosting N_2, O_2 and CH_4,[17] and (+)-cage *syn*-**7**, which can selectively bind gases like acetylene with respect to ethylene and ethane.[18]

The first synthetic approach to benzotricamphor *syn*-**5** was the oxidation of benzotriborneol *syn*-**4**.[17] Alternatively, benzotricamphor *syn*-**5** can be obtained by acid hydrolysis of its tris(ethanediol acetal), preparation of which has been described.[19] These methodologies suffer from the need for stannylated starting material and several protection/deprotection steps for the copper-mediated cyclotrimerization reaction. To shorten the synthetic route, skipping the stannylation step and improving the final yields, an alternative Heck-type cyclotrimerization strategy[20] has been applied. A suitable building block for the cyclotrimerization was obtained in three steps (Scheme 1) starting from hydrazone **8**,[15,21] which was iodinated in the presence of *N*,*N*,*N*,*N*-tetramethylguanidine (TMG)[22] to furnish the corresponding vinyl iodide **9**. The latter was oxidized with pyridinium dichromate,[23] tetrabutylammonium perruthenate/*N*-methylmorpholine *N*-oxide (NMO)[24] or more conveniently with a catalytic amount of ruthenium(III) chloride and NMO in acetonitrile.

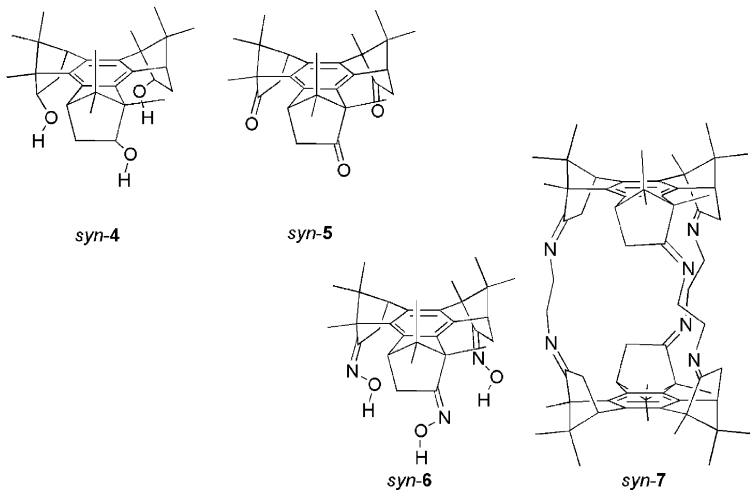


8 **9** **10**

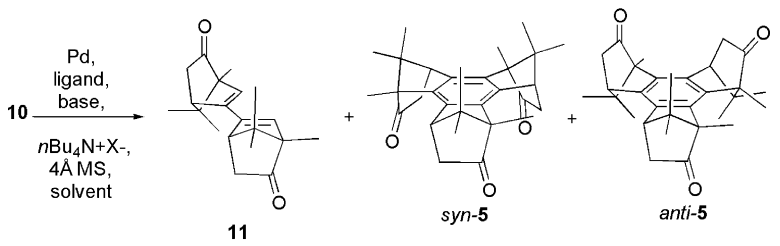
Scheme 1. Preparation of **10** for Heck-type cyclotrimerization. a) I_2, TMG, Et_2O, RT (86% yield); b) $RuCl_3 \cdot H_2O$ (3 mol%), NMO, MeCN, RT (87% yield).

Substrate **10** can be directly employed for palladium-mediated cyclotrimerization leading to the desired benzocyclotrimeric product *syn*-**5**. The relevant modifications to this methodology introduced by Sakurai et al.,[20a,b] consisting of the use of considerable amounts (1000 mol%) of tetrabutylammonium acetate to stabilize palladium nanoclusters,[25] turned out to be unsatisfactory in our case. Under such conditions, substrate **10** afforded a highly favourable 5:1 *syn*-to-*anti* ratio of cyclotrimers **5**, but with a modest overall yield of 18% (Scheme 2). This is partially imputable to the concomitant formation of significant amounts (17% yield) of dimer **11**, formed by homocoupling of iodide **10**. This reaction pathway probably involves a palladium(IV) intermediate,[20c] which can be reintroduced into the catalytic cycle by acetate ion acting as a reducing agent.[26]

The cyclotrimerization reaction of **10** was screened by varying several reaction parameters to improve the selectivity and final yield of *syn*-**5** (Table 1). To reduce the amount of waste we considerably decreased the amount of tetrabutylammonium ion to five equivalents (Table 1). Initial screening of different bases (Table 1, entries 1–4) with PPh_3 as ligand evidenced the higher efficiency of potassium carbonate, which enabled formation of *syn*-**5** (16%), although dimer **11** was also produced as major product (59%). Subsequent ligand screening (Table 1, entries 5–7) showed that, among bidentate chelating diphosphines, 1,1′-bis(diphenylphosphino)ferrocene (dppf) was the most effec-



syn-4 *syn*-5 *syn*-6 *syn*-7



Scheme 2. Palladium-catalyzed cyclotrimerization of vinyl iodide **10**. Reagents and conditions are described in Table 1.

Table 1. Effect of base, ligand, solvent, Pd^{II} source and additives on the cyclotrimerization reaction of **10**.[a]

Entry	Base (5 equiv)	Ligand[b]	X in nBu_4NX[c] (5 equiv)	Solvent	Pd source (5 mol %)	Additive (5 equiv)	*syn*-**5** [%][d]	*anti*-**5** [%][d]	**11** [%][d]
1	Na_2CO_3	PPh_3	OAc	dioxane	$Pd(OAc)_2$	–	12	2	48
2	K_2CO_3	PPh_3	OAc	dioxane	$Pd(OAc)_2$	–	16	3	59
3	Cs_2CO_3	PPh_3	OAc	dioxane	$Pd(OAc)_2$	–	5	1	24
4	K_3PO_4	PPh_3	OAc	dioxane	$Pd(OAc)_2$	–	10	2	32
5	K_2CO_3	dppe	OAc	dioxane	$Pd(OAc)_2$	–	18	4	36
6	K_2CO_3	dppp	OAc	dioxane	$Pd(OAc)_2$	–	22	4	49
7	K_2CO_3	dppf	OAc	dioxane	$Pd(OAc)_2$	–	28	6	43
8	K_2CO_3	dppf	Br	dioxane	$Pd(OAc)_2$	–	0	0	13
9	K_2CO_3	dppf	I	dioxane	$Pd(OAc)_2$	–	0	0	4
10	K_2CO_3	dppf	OAc	toluene	$Pd(OAc)_2$	–	38	7	30
11	K_2CO_3	dppf	OAc	toluene	$[Pd_2(dba)_3]$[e]	–	7	1	30
12	K_2CO_3	dppf	OAc	toluene	$PdCl_2$	–	30	6	19
13	K_2CO_3	dppf	OAc	toluene	$Pd(OAc)_2$	NaOAc	53	11	17
14	K_2CO_3	dppf	OAc	toluene	$Pd(OAc)_2$	KOAc	65	13	19

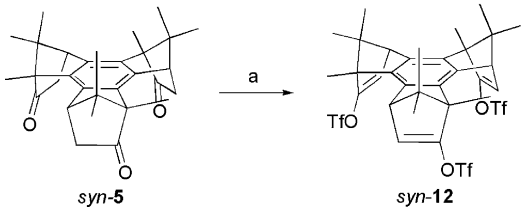
[a] All reactions were carried out in the presence of powdered 4 Å molecular sieves at 100 °C for 4 h. [b] 10 (entries 1–7) or 5 mol % (entries 8–19). [c] $Bu_4N^+OAc^-$ was conveniently prepared in situ from stoichiometric amounts of $Bu_4N^+I^-$ and AgOAc. [d] Yields were determined by GC for an average of two runs with tetradecane as internal standard. [e] dba = *trans,trans*-dibenzylideneacetone.

tive ligand, affording *syn*-**5** in 28 % yield, even though a large amount of dimer **11** was still formed. The positive effect of employing large amounts of acetate ion[27] to effectively promote the Heck-type catalytic cycle was confirmed when bromide or iodide was used as counterion for tetrabutylammonium (Table 1, entries 8 and 9), which produced exclusively small amounts of dimer **11**. The use of toluene, as an apolar and noncoordinating solvent (Table 1, entries 10 and 7), afforded better yields of *syn*-**5**, concomitant with a smaller amount of dimer **11**.

Subsequent screening of different palladium sources confirmed the superior catalytic activity of palladium(II) acetate (Table 1, entries 11 and 12). Finally, the amount of acetate ion in the reaction medium was increased by addition of the corresponding inexpensive sodium or potassium salt (Table 1, entries 13 and 14), which led to the best yields of benzocyclotrimer *syn*-**5** and reduced considerably the amount of dimer **11**. This result confirms the pivotal role played by the acetate ion in the coupling reaction, which is probably related to its contribution to stabilizing palladium nanoclusters.[25–27] Experiments carried out with potassium acetate in the absence of tetrabutylammonium acetate did not provide the desired product, while reactions with larger amounts of ammonium acetate did not improve the yield of *syn*-**5** with respect to data reported in Table 1, entry 14. Optimized conditions were finally applied to multigram-scale reactions (30 mmol) affording a reproducible 58 % yield of isolated *syn*-**5**, which was easily obtained in pure form by recrystallization of the crude reaction mixture and flash chromatography of the mother liquors.

Benzotricamphor *syn*-**5** was conveniently converted to the corresponding tris-enol triflate intermediate derivative with potassium hexamethyldisilazide (KHMDS),[28] which was treated with *N*-phenylbis(trifluoromethanesulfonimide)[29] to give a reproducible 83 % yield of tris-triflate **12** (Scheme 3).

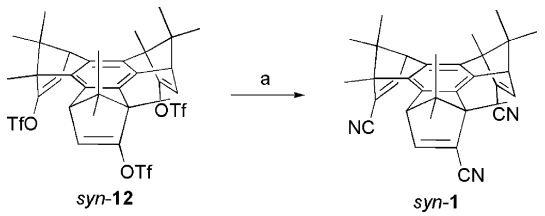
Substitution of the triflate group on vinyl residues is common practice with well-established coupling procedures based on the use of palladium catalysis (Heck,[30] Stille,[31] Negishi,[32] Suzuki,[33] etc.). In the case of benzotricamphor tris(enol triflate) *syn*-**12**, substitution proved ineffective, or at best incomplete, when simple



Scheme 3. Conversion of tris-ketone *syn*-**5** to tris-triflate *syn*-**12**. a) i) KHMDS, THF, −78 °C; ii) $PhNTf_2$, −78 °C→RT (83 % overall yield).

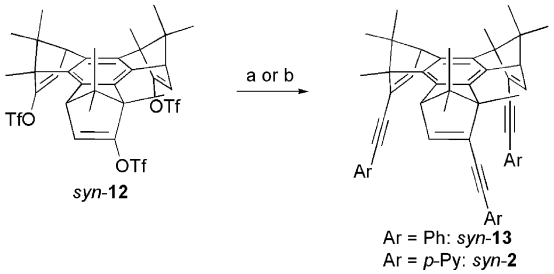
tributyltin-, bromomagnesium- or pinacolborate-benzene was used as nucleophile in the presence of several suitable palladium(0) precursors and ligands. The poor reactivity of the substrate was attributed to the high steric hindrance exerted by the three bridgehead methyl groups close to the triflate moieties. Indeed, smaller nucleophiles, such as cyanide[34] from trimethylsilyl cyanide (TMSCN), in the presence of $[Pd(PPh_3)_4]$ led to exhaustive substitution of all three positions and afforded benzotricamphor tris-nitrile *syn*-**1** in good yield (78 %, Scheme 4).

To introduce three aryl groups on the benzo tris-bornene scaffold, the steric hindrance present in such a compound suggested employment of linear narrow spacers, such as an ethynediyl moiety. The reaction of phenylacetylene with



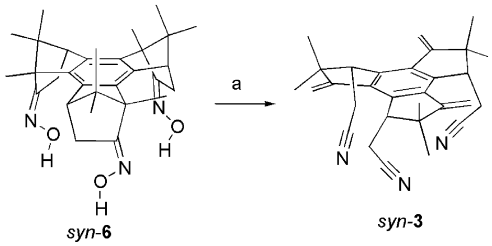
Scheme 4. Conversion of tris-triflate *syn*-**12** to the corresponding tris-nitrile *syn*-**1**. a) TMSCN, $[Pd(PPh_3)_4]$ (5%), ET_3N/NMP, 110°C (78% yield).

syn-**12** under modified Sonogashira[35] conditions afforded good yields (85%) of tris-substituted alkynyl arene *syn*-**13**. Synthesis of a tris-ethynyl-*p*-pyridine-substituted benzocyclotrimer under similar experimental conditions finally gave tridentate ligand *syn*-**2** in satisfactory yield (84%) from 4-pyridylacetylene (Scheme 5).[36]



Scheme 5. Conversion of tris-triflate *syn*-**12** to the corresponding tris-arylethynyl derivatives *syn*-**13** and *syn*-**2**. a) PhC≡CH, piperidine, $Pd(OAc)_2$ (10%), PPh_3 (20%), toluene, 60°C (85% yield); b) 4-PyC≡CH, piperidine, $Pd(OAc)_2$ (10%), PPh_3 (20%), toluene, 60°C (84% yield).

A different, more flexible tridentate tris-nitrile ligand, namely, *syn*-**3**, was obtained in high yield by threefold Beckmann-like ring opening[37] of trioxime *syn*-**6** (Scheme 6), which was previously obtained by us.[17] The reaction, which



Scheme 6. a) MsCl, Py, 0→25°C (92% yield).

operates efficiently on each oxime moiety, leads to rupture of the bicyclic structure and formation of terminal alkyl nitrile moieties and 1,1-disubstituted alkenes, while maintaining the chirality of the molecule and its C_3 symmetry.

The coordinating properties of the tridentate scaffolds *syn*-**1**, *syn*-**2** and *syn*-**3** with silver(I) and platinum(II) centres having different coordination geometries were investigated. The resulting supramolecular metal–ligand capsules were characterized structurally with the aid of 1D and 2D NMR spectroscopy and ESI-MS techniques.

Self-assembly of tridentate ligands *syn*-1, *syn*-2 and *syn*-3 with silver(I): Few examples of nitrile-based metal–ligand capsules are known in the literature. Dalcanale and coworkers reported the synthesis of resorcin[4]arene scaffolds bearing four nitrile units held together by Pd^{II} or Pt^{II} corners.[38] More recently, heterodimeric capsules of formula $L_{Py}M_4L_{CN}$ were selectively obtained from tetrapyridine (L_{Py}) and tetranitrile (L_{CN})ligands with Pt^{II} or Pd^{II}, by exploiting the different coordination abilities of the two metal centres in combination with different steric requirements.[39]

The behaviour of flexible tris-nitrile ligand *syn*-**3** was investigated by NMR titration of a solution of the ligand in $CDCl_3$ with a solution of AgOTf in $[D_6]$acetone. The spectra showed progressive downfield shift of the diastereotopic methylene protons connected to the nitrile moiety under fast exchange on the NMR timescale,[40] indicating coordination of the functional group to silver atoms (Figure 1). The maximum chemical shift variation was achieved at a

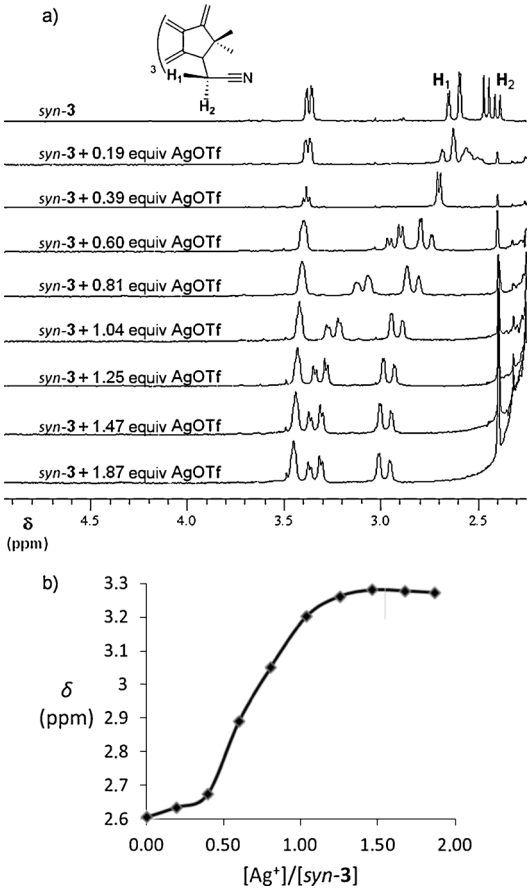


Figure 1. a) Portion of the ^1H NMR spectra in $CDCl_3$ for the titration of tris-nitrile *syn*-**3** with AgOTf. b) Titration curve for tris-nitrile *syn*-**3** with AgOTf.

[Ag]:[*syn*-**3**] ratio slightly greater than 1:1, and Job plot analysis finally confirmed the 1:1 stoichiometry between ligand and metal. This supports formation of a complex in which the tridentate C_3-symmetric ligand *syn*-**3** chelates a single silver(I) cation in a tetrahedral geometry with a coordination site possibly occupied by a water molecule or counteranion (see the Supporting Information). The ^{1}H NMR spectrum at a [Ag^I]:[*syn*-**3**] ratio of 0.39 is of particular interest, because it seems that the formed aggregate loses the chirality imparted by the benzocyclotrimer scaffold, since the diastereotopic protons on the methylene unit connected to the nitrile moiety give rise simply to a doublet. Moreover, the initial smooth slope of the titration curve of *syn*-**3** with Ag^I drastically increased above a [Ag]:[*syn*-**3**] ratio of 0.5. Both phenomenon cannot be easily interpreted, but they could be ascribable to the flexible structure of the ligand *syn*-**3** together with the presence of several coordinating nitrile moieties undergoing exchange phenomena at the Ag^I centre. However, when the degrees of freedom are reduced by further addition of metal, the positions of observed nuclei are more univocally determined and marked differences in chemical shift variations can be observed. Despite this, the robustness of the final complex $[Ag_3(syn\text{-}\mathbf{3})_2]^{3+}$ is limited by the unfavourable geometry of the ligand (as deducible by the poor resolution of the fine couplings of the methylene moiety) and it is too labile to survive the mildest ESI analysis conditions that were used in an attempt to better investigate the structure of the assembly.

Similarly, when a solution of AgOTf in [D_6]acetone was added portionwise to a solution of the more rigid tris-nitrile *syn*-**1** in $CDCl_3$, a downfield shift of the vinyl proton was observed in the NMR spectra (Figure 2), indicating coordination of the nitrile moiety to Ag^I cations. The chemical shift of the vinyl proton changed gradually with increasing amount of Ag^I under fast exchange on the NMR timescale, moving from $\delta = 7.40$ ppm for the free ligand to $\delta = 7.80$ ppm when the [Ag^I]:[*syn*-**1**] ratio reached 3:2 (Figure 2). This ratio is consistent with the formation of a strained complex in which two benzocyclotrimeric units are held together by three metal centres, or with a less tensioned structure in which four ligands occupy the vertices of a weakly distorted tetrahedron assembled with six Ag^I cor-

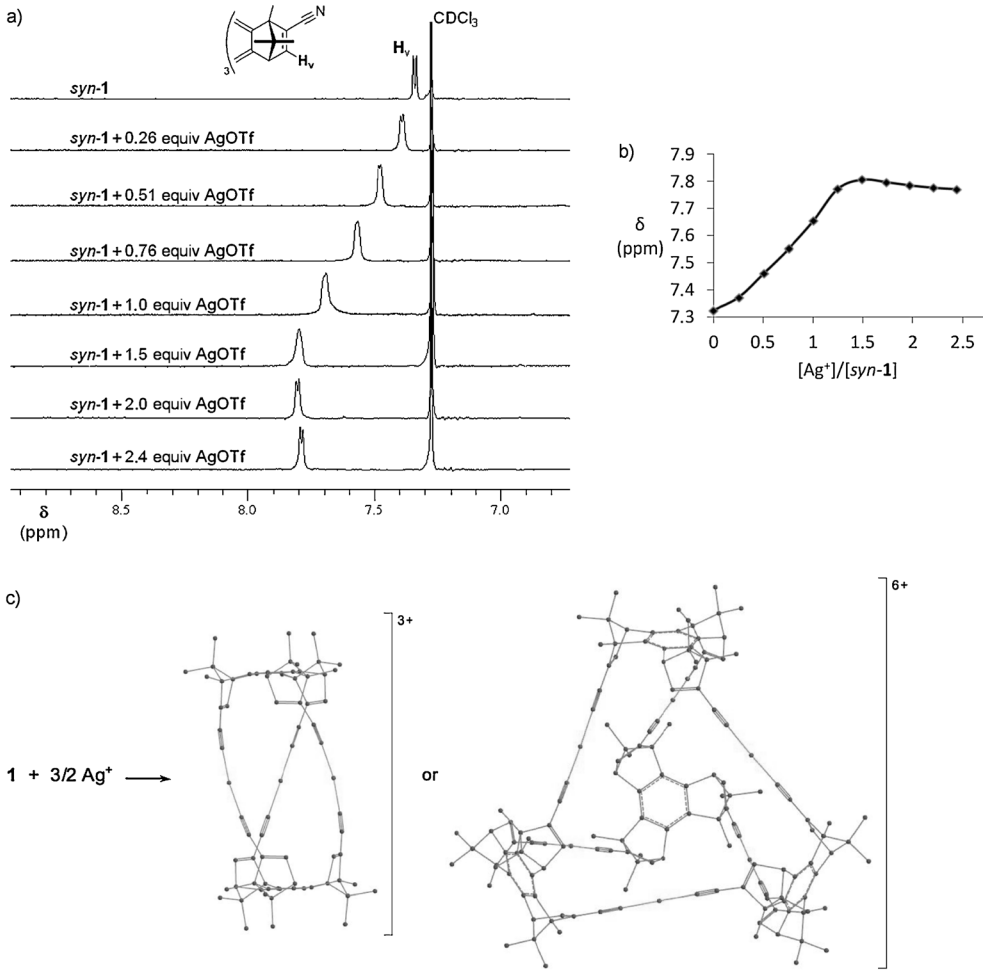


Figure 2. a) Portion of the ^{1}H NMR spectra for the titration in $CDCl_3$ of tris-nitrile *syn*-**1** with AgOTf. b) Titration curve for tris-nitrile *syn*-**1** with AgOTf. c) Pictorial representation of the possible aggregates $[Ag_3(syn\text{-}\mathbf{1})_2]^{3+}$ (left) and $[Ag_6(syn\text{-}\mathbf{1})_4]^{6+}$ (right).

ners. The fact that further addition of silver did not change significantly the chemical shift of the vinyl protons indicated formation of a stable aggregate.

Very small differences in ^{19}F NMR shifts were observed between coordinated and uncoordinated AgOTf, that is, this weakly coordinating fluorinated anion does not participate in formation of the assembly and presumably does not reside within the cavity of the concave aggregate. Indeed, in one case the cavity is too small and improperly shaped, so that the anion is left outside; in the other case, the empty space inside the cage is very large, but also unconfined, and triflate can easily pass through the wide open windows of the structure, as deduced by molecular modelling[41] (Figure 2).

Mass spectrometry is a valuable analytical tool for investigating metal-based supramolecules because of the cationic nature of the metal-containing aggregates.[42] To gain further insight into the structure of the metal–ligand capsules, samples of the 3:2 complex between Ag^I and *syn*-**1** in dilute methanol solution were subjected to ESI-MS analysis in the range *m*/*z* 100–2000. Characteristic peaks with the expected isotopic clusters were observed at *m*/*z* 1565.6 and 707.3, corresponding to monocationic complex $[Ag_3(syn\text{-}\mathbf{1})_2(OTf)_2]^+$ and dicationic complex $[Ag_3(syn\text{-}\mathbf{1})_2(OTf)]^{2+}$. Further peaks at *m*/*z* 1307.3 and 580.4 (mono- and dicationic species of $Ag_2(syn\text{-}\mathbf{1})_2$, respectively, related to the same molecule with the loss of a silver corner) were present. Such peaks could also arise from the structure $[Ag_6(syn\text{-}\mathbf{1})_4]^{6+}$, or even multiple aggregates, but the lack of diagnostic peaks with *m*/*z* 993.6 or 536.5, related to tricationic $[Ag_6(syn\text{-}\mathbf{1})_4(OTf)_3]^{3+}$ and pentacationic $[Ag_6(syn\text{-}\mathbf{1})_4(OTf)]^{5+}$ complexes, and any of the peaks related to aggregate $Ag_5(syn\text{-}\mathbf{1})_4$, demonstrates formation in solution of the dimeric capsule $Ag_3(syn\text{-}\mathbf{1})_2$ (Figure 3).

In comparison with a nitrile moiety, pyridine is a more strongly coordinating ligand that has been widely employed for the creation of supramolecular architectures.[4e, k, 43] Coordination of *syn*-**2** with silver(I) was investigated by means of NMR titration, by observing the downfield shift of the signals assigned to the of vinyl and pyridine protons (Figure 4). A linear profile of the chemical shift of such resonances versus the [Ag]:[*syn*-**2**] ratio was observed, with a marked change in slope above an [Ag]:[*syn*-**2**] ratio of 1.5 (Figure 4). This stoichiometry is in agreement with $[Ag_3(syn\text{-}\mathbf{2})_2](OTf)_3$, $[Ag_6(syn\text{-}\mathbf{2})_4](OTf)_6$, or any multiple aggregate thereof.

Evidence for the actual stoichiometry and geometrical features of the resulting complex arose from ESI analysis of the correct 2:3 mixture of ligand *syn*-**2** and silver(I) triflate. Indeed, observed peaks with *m*/*z* 2022.2, 936.6, and 575.0 can be associated with $[Ag_3(syn\text{-}\mathbf{2})_2(OTf)_2]^+$, $[Ag_3(syn\text{-}\mathbf{2})_2$-

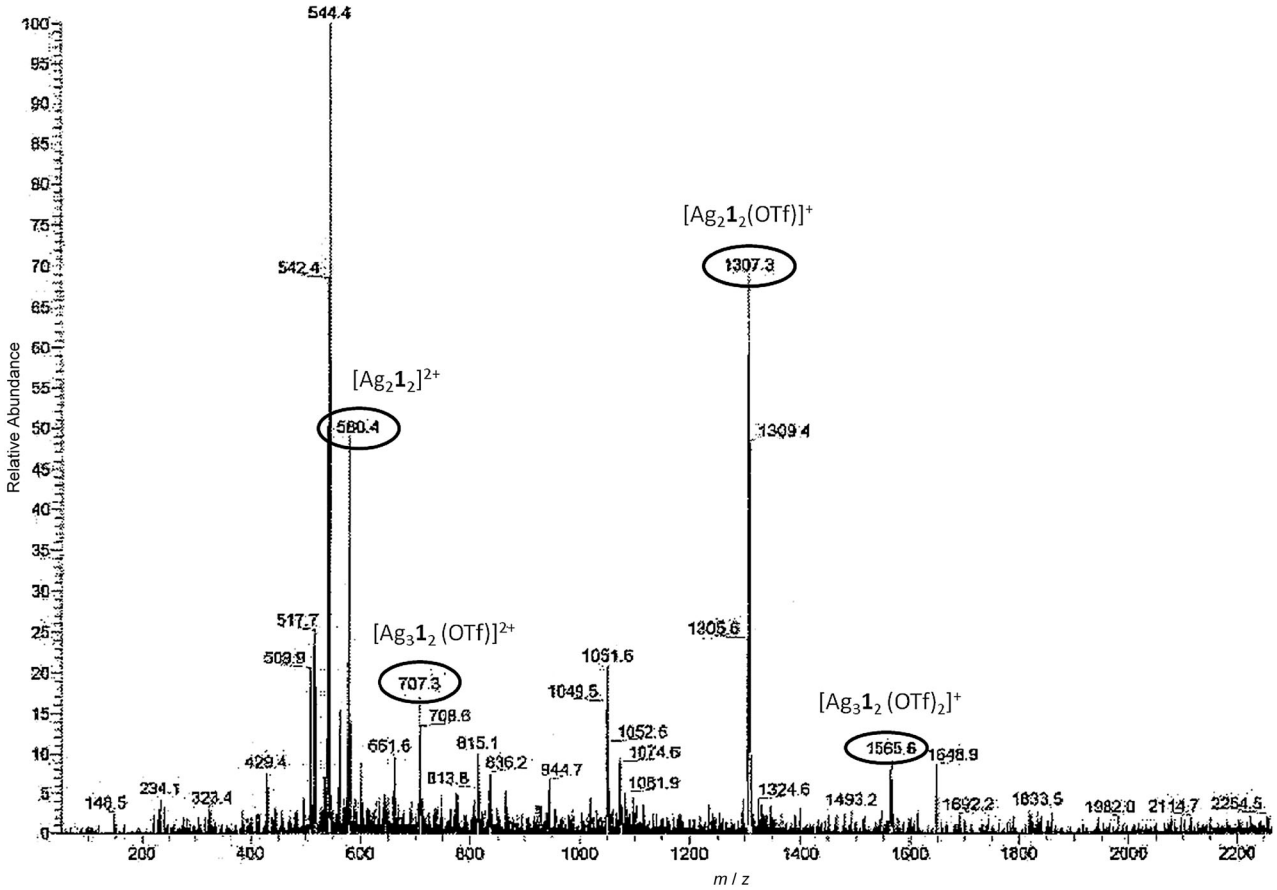


Figure 3. ESI mass spectrum of $[Ag_3(syn\text{-}\mathbf{1})_2](OTf)_3$.

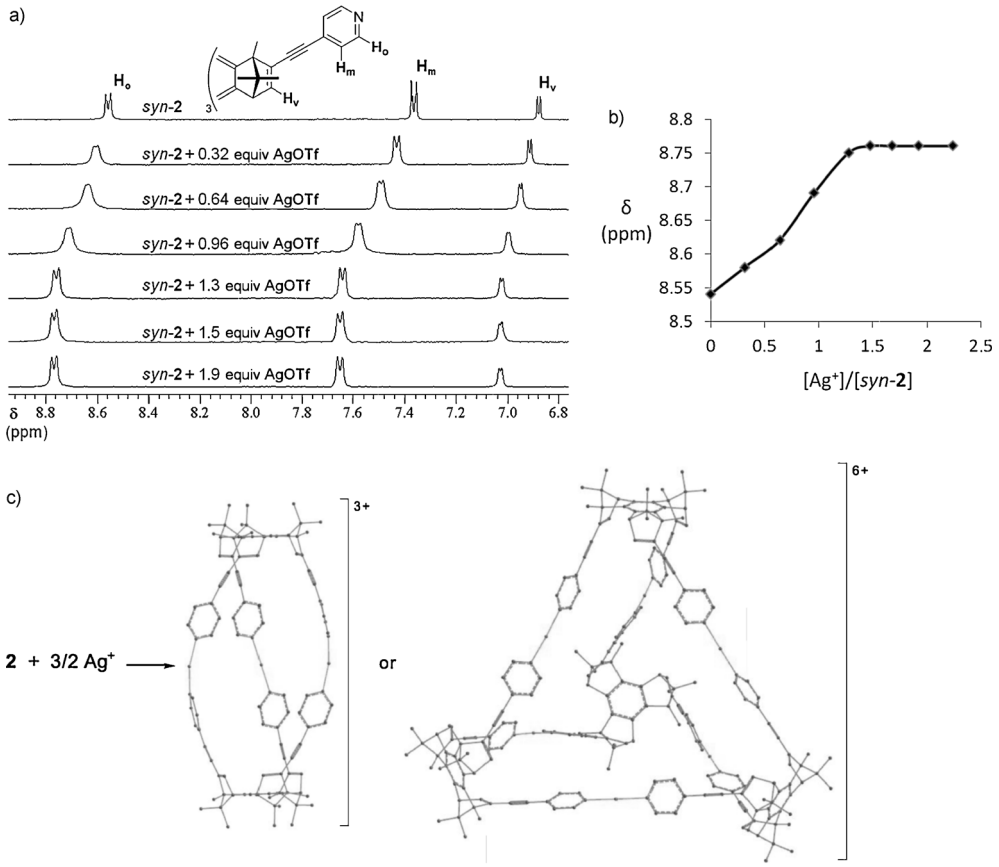


Figure 4. a) Portion of the ^{1}H NMR spectra for the titration in [D_6]acetone of tris-pyridine *syn*-**2** with AgOTf. b) Titration curve for tris-pyridine *syn*-**2** with AgOTf. c) Pictorial representation of the possible aggregates $[Ag_3(syn\text{-}\mathbf{2})_2]^{3+}$ and $[Ag_6(syn\text{-}\mathbf{2})_4]^{6+}$.

$(OTf)]^{2+}$, and $[Ag_3(syn\text{-}\mathbf{2})_2]^{3+}$ respectively, as well as *m*/*z* 1764.2 to $[Ag_2(syn\text{-}\mathbf{2})_2(OTf)]^{+}$ and *m*/*z* 1509.5 to $[Ag(syn\text{-}\mathbf{2})_2]^{+}$. Larger aggregates are excluded, since no peaks that are diagnostic for such species were observed at *m*/*z* 1296 and 718 corresponding to the tri- and pentacationic $[Ag_6(syn\text{-}\mathbf{2})_4(OTf)_n]^{(6-n)+}$, as well as $[Ag_5(syn\text{-}\mathbf{2})_4(OTf)_n]^{(6-n)+}$ species with *m*/*z* 1891, 1211, and 871 (Figure 5).

Self-assembly of tridentate *syn*-1, *syn*-2 and *syn*-3 with platinum(II): The typical square-planar geometry of *cis*-chelated platinum(II) is suitable for connecting two or more multidentate ligands with a 90° reciprocal orientation. First NMR titration experiments of nitrile-based ligands *syn*-**1** and *syn*-**3** with [Pt(dppp)$(OTf)_2$] (dppp = 1,3-bis(diphenylphosphino)-propane) or [Pt(dippe)$(OTf)_2$] (dppe = 1,2-bis(diisopropylphosphino)ethane) provided no evidence for the formation of complexes with a defined metal:ligand stoichiometry and suggested formation of multiple aggregates through a disordered coordination process, in which oligomeric aggregates are likely formed rather than well-organized metal–ligand coordination cages. Similar results were confirmed by ESI-MS analysis, which did not show the formation of any defined dimeric or multimeric larger aggregates in solution, either in methanol or chloroform as solvent. The lack of coordination of *syn*-**1** and *syn*-**3** with these *cis*-platinum(II) complexes is probably imputable to the poor coordinating ability of nitriles and the competitive effect exerted by the solvent or the vinyl groups in the case of ligand *syn*-**3**.

The strong coordinating ability of pyridine[2l] has been extensively exploited for the preparation of self-aggregating capsules[4] and cavitands,[3] especially with Pd^{II} centres. Titration of *syn*-**2** with [Pt(dppp)$(OTf)_2$] in [D_6]acetone led to new downfield resonances in the NMR spectra, the relative intensity of which increased concomitantly with the decrease of the signals of free *syn*-**2**, which completely disappeared in correspondence to a 3:2 stoichiometric ratio between Pt^{II} and *syn*-**2** (Figure 6).

The free and bound ligand are in slow exchange on the NMR timescale, which is a common finding for pyridine-based supramolecular architectures with Pd^{II} or Pt^{II} centres. The appearance of only two sets of NMR signals attributed to free and coordinated ligand during the titration implies that the new signals are ascribable to a C_3-symmetric chiral complex, which means that the mono- and dicoordinate complexes are not observed and the formation of the fully closed capsule is preferred (Figure 6). ^{31}P NMR analysis further confirmed the C_3 symmetry of metal capsule $[Pt_3(syn\text{-}\mathbf{2})_2(dppp)_3](OTf)_6$. The resonance attributed to free [Pt(dppp)$(OTf)_2$] in CD_3OD at $\delta = -12.96$ ppm with a $^1J_{P-Pt}$ value of 3675 Hz moved upfield upon coordination of the ligand *syn*-**2** with a new resonance at $\delta = -13.92$ ppm with a $^1J_{P-Pt}$ value of 3040 Hz, while the free [Pt(dippe)$(OTf)_2$] in

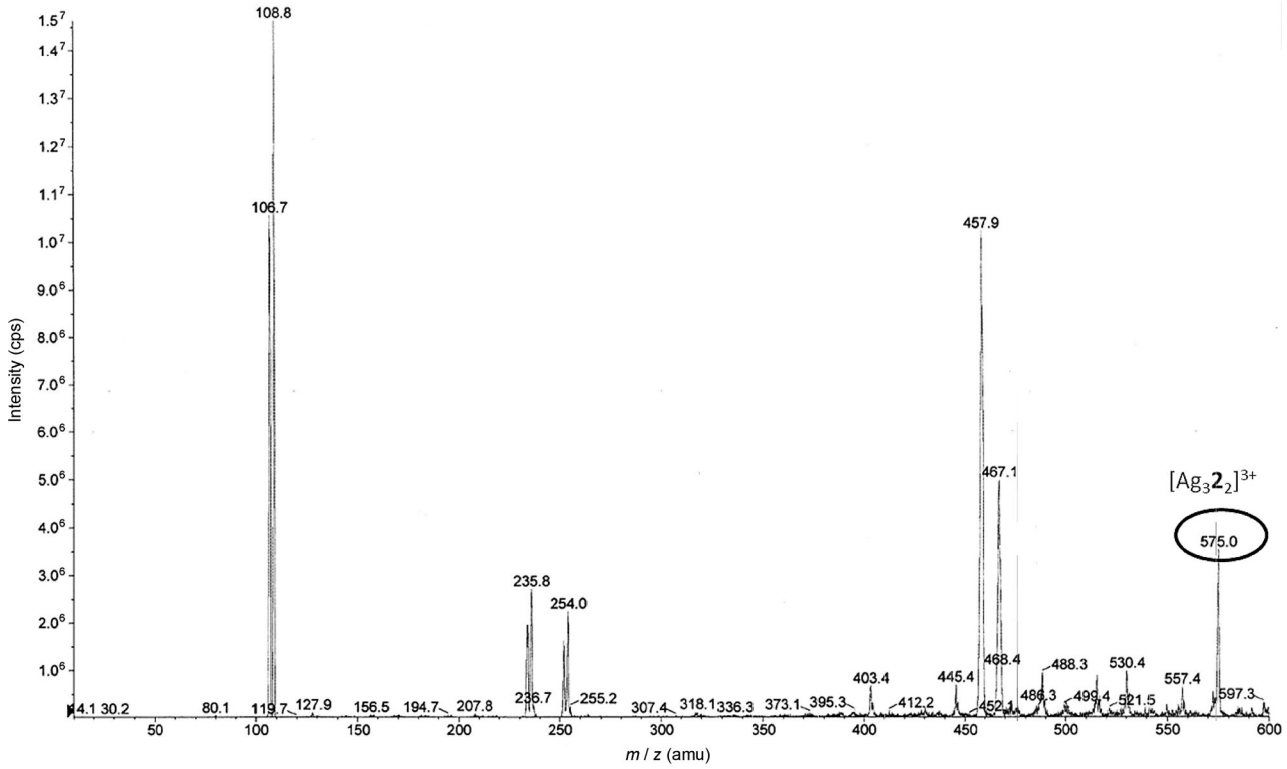


Figure 5. ESI mass spectra of $[Ag_3(syn\text{-}\mathbf{2})_2](OTf)_3$.

CD_3OD at $\delta = 70.95$ ppm with a $^1J_{P-Pt}$ value of 3791 Hz moved upfield upon coordination of ligand *syn*-**2** with a new resonance at $\delta = 65.7$ ppm having $^1J_{P-Pt}$ value of 3129 Hz. In both cases at a Pt:*syn*-**2** ratio of 3:2 a single resonance for all of the P atoms is observed, which confirms the C_3 symmetry of the formed assembly, while the value of the coupling constant between P and the Pt^{II} metal centre is typical for a complex with pyridine residues coordinated *trans* to the P atoms.[44]

Formation of the coordination capsule was further evidenced by 2D NOESY NMR experiments. In the case of $[Pt_3(syn\text{-}\mathbf{2})_2(dppp)_3](OTf)_6$, NOE interactions between H_{ortho} of the pyridine groups of *syn*-**2** and the phenyl residues of the dppp ligand were observed (Figure 7). Analogous dipolar interactions are observed in the complex $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_6$ obtained by mixing *syn*-**2** and $[Pt(dippe)](OTf)_2$ in a 2:3 ratio. Clear cross-peaks are observed between H_{ortho} of the pyridine residues of the benzocyclotrimer and the isopropyl resonances of the diphosphine ligand coordinated to Pt^{II} (see the Supporting Information). Further evidence on coordination of the tridentate ligand with Pt^{II} precursors is provided by DOSY experiments[45] (see the Supporting Information). The free $[Pt(dippe)](OTf)_2$ complex and *syn*-**2** in CD_3OD show similar diffusion coefficients (1.4×10^{-9} cm^2s^{-1}), while the dimeric capsule $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_6$ shows a marked decrease of the diffusion coefficient (7.9×10^{-10} cm^2s^{-1}). The reciprocal of the ratio between the two diffusion coefficients provides an estimation of the ratio between the hydrodynamic radii of the dimeric capsule and monomeric *syn*-**2**.[45] The obtained value of 1.8 is in agreement with doubling of the size of *syn*-**2** when two ligand molecules assemble to form the dimeric capsule $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_6$.

Mass spectrometric analysis was performed on a solution of $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_6$, since the molecular weight of the similar complex $[Pt_3(syn\text{-}\mathbf{2})_2(dppe)_3](OTf)_6$ exceeds the mass range of the instrument employed. The ESI-MS analysis of a preformed acetone solution containing a 2:3 mixture of *syn*-**2** and $[Pt(dippe)](OTf)_2$ further diluted in methanol showed unambiguously the formation of $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_6$ (Figure 8), as confirmed by the presence of peaks at *m*/*z* 1685.6, 1073.1, 768.5 and 584.1, which can be attributed to $\{[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_4\}^{2+}$, $\{[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_3\}^{3+}$, $\{[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_2\}^{4+}$ and $\{[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)\}^{5+}$, respectively. The MS spectra also show the presence of complexes held together by two and even only one platinum corner, as evidenced by peaks at *m*/*z* 1305.4, 822.1 and 579.2, which can be assigned to $\{[Pt_2(syn\text{-}\mathbf{2})_2(dippe)_2](OTf)_4\}^{2+}$, $\{[Pt_2(syn\text{-}\mathbf{2})_2(dippe)_2](OTf)\}^{3+}$ and $\{[Pt_2(syn\text{-}\mathbf{2})_2(dippe)_2](OTf)_2\}^{4+}$, as well as *m*/*z* 929.4 related to $[Pt(syn\text{-}\mathbf{2})_2(dippe)]^{2+}$. Peaks diagnostic of larger aggregates were not observed, and this confirms exclusive formation in solution of dimeric capsules of finite geometry, owing to preorganization of the rigid coordinating pyridine moieties. As a further confirmation of the $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_6$ stoichiometry, MS-MS analysis (Supporting

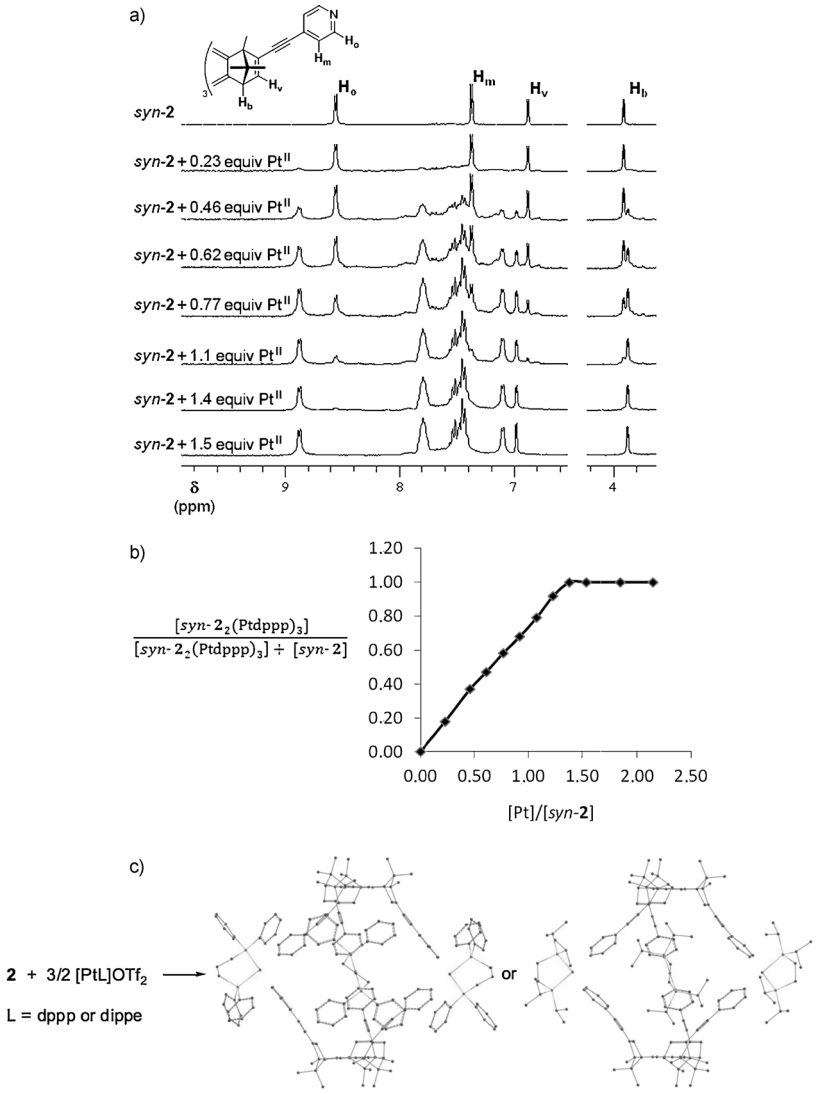


Figure 6. a) Portions of the ^{1}H NMR spectra for the titration of tris-pyridine *syn*-**2** in [D_6]acetone with [Pt(dppp)(OTf)$_2$]. b) Titration curve for tris-pyridine *syn*-**2** with [Pt(dppp)]OTf$_2$. c) Pictorial representation of the complexes $[Pt_3(syn\text{-}\mathbf{2})_2(dppp)_3]^{6+}$ and $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3]^{6+}$.

Information) revealed that a peak with *m*/*z* 1685.6 attributed to $\{[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_4\}^{2+}$ showed subsequent loss of one Pt^{II} corner to give initially a peak at 1306.9 $\{[Pt_2(syn\text{-}\mathbf{2})_2(dippe)_2](OTf)_2\}^{2+}$. Thus, at low energy the assembly expels only one Pt^{II} corner, while at high energy the aggregate disassembles, leading to a peak at 607.3, corresponding to $\{[Pt_2(syn\text{-}\mathbf{2})_2(dippe)_2](OTf)\}^{+}$. Higher aggregates are expected to lose a larger number of Pt^{II} corners before disassembly occurs.

Conclusion

A new methodology for the preparation of (+)-*syn*-benzotricamphor *syn*-**5** in high yield and with good selectivity was described, based on palladium-catalyzed cyclotrimerization of enantiopure iodobornene **10**. The Heck-type cyclotrimerization approach reduced the number of synthetic steps compared to previous methodologies and led to an increased overall yield by avoiding protection/deprotection steps and the use of toxic organotin compounds. The reaction between the tris-enolate of the benzotricamphor with *N*-phenyl-bis(trifluoromethanesulfonimide) afforded the corresponding tris-trifluoromethanesulfonate derivative *syn*-**12**, which was conveniently functionalized by coupling reactions with trimethylsilyl cyanide and 4-ethynylpyridine.

New benzocyclotrimers *syn*-**1** and *syn*-**2** were used as ligands for silver(I) and platinum(II) centres to prepare coordination cages of general formula L_2M_3 based on metal–ligand interactions. Tris-nitrile *syn*-**1** coordinated efficiently to silver to produce a well-defined coordination cage, while disordered oligomers were observed with platinum. The stronger coordination ability of tris-pyridine *syn*-**2** allowed preparation of complexes with well-defined stoichiometry, both with Ag^I and with Pt^{II} precursors. Formation of the corresponding complexes and the relative stoichiometry were studied and confirmed with the aid of NMR and ESI-MS techniques.

Several attempts were made to find suitable guests for the smaller capsule $[Ag_3(syn\text{-}\mathbf{1})_2](OTf)_3$ by testing a wide range of gaseous guests with appropriate molecular volume, such as methane, ethane, ethylene and acetylene, or liquid guests like CH_3I and CH_2Cl_2. Similarly, capsules $[Ag_3(syn\text{-}\mathbf{2})_2](OTf)_3$ and $[Pt_3(syn\text{-}\mathbf{2})_2(dppp)_3](OTf)_6$ did not show evidence of encapsulation of aromatic guests such as *p*-xylene, phenylacetylene and 1,4-phenyldiacetylene, which are expected to provide good CH–π contacts with the electron-rich aromatic surface of the benzocyclotrimer scaffold.[18]

Attempts to make such metal–ligand capsules water-soluble are currently underway in order to exploit the hydrophobic effect to achieve encapsulation and possibly enantioselective recognition.

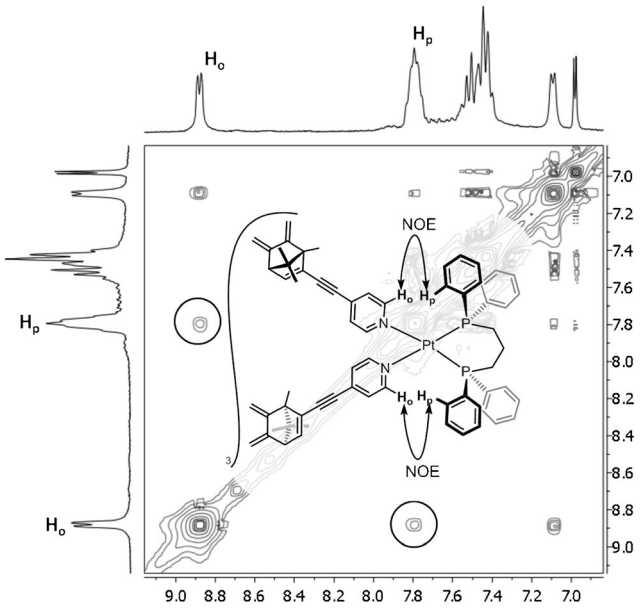


Figure 7. NOESY spectrum of $[Pt_3(syn\text{-}\mathbf{2})_2(dppp)_3](OTf)_6$ in $[D_4]$MeOH showing the cross-peaks between the pyridine residues of the benzocyclotrimer and the phenyl residues of the diphosphine ligand coordinated to Pt^{II}.

Experimental Section

General: Reactions were carried by standard techniques in flame-dried glassware cooled under argon. Commercial high-purity reagents were employed without further purification. Dry THF and Et_2O were distilled prior to use from sodium/benzophenone. Dichloromethane was distilled prior to use from calcium hydride. The progress of the reactions was monitored by TLC, GC-MS or ^{1}H NMR spectroscopy. ^{1}H, ^{13}C{^{1}H} and ^{31}P{^{1}H} NMR spectra were recorded at 298 K, unless otherwise stated, on a Bruker AVANCE 300 spectrometer operating at 300.15, 75.48 and 122.5 MHz, respectively, and the δ values in parts per million (ppm) are relative to TMS and H_3PO_4. ^{19}F NMR spectra were recorded at 298 K on a Bruker AC 200 spectrometer operating at 188.2 MHz and the δ values in ppm are relative to $CFCl_3$. GC analyses were performed with a 30 m, 0.25 mm i.d., Rtx-5MS capillary column (5:95 diphenyl:dimethylpolysiloxane). Flash-chromatographic purification was performed with 230–400 mesh silica gel Merck 60. Melting points are uncorrected. Optical rotations were measured in a 10 cm cell.

(1*S*,2*R*,4*S*)-5-Iodo-2-hydroxy-1,7,7-trimethylbicyclo[2.2.1]hept-5-ene (9): A solution of 2-hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-5-hydrazone (**7**; 11.20 g, 61.4 mmol) and TMG (48 mL, 382 mmol) in dry Et_2O (100 mL) was added over 30 min to a solution of I_2 (31.75 g, 125 mmol) and TMG (30 mL, 239 mmol) in dry Et_2O (200 mL) at room temperature. The resulting slurry was concentrated at reduced pressure, H_2O (150 mL) was added and the mixture was extracted with hexane (5×100 mL). The combined organic layers were washed with 1 M aqueous HCl (50 mL) and saturated aqueous NaCl (50 mL), dried over $MgSO_4$ and concentrated in vacuo. The residual oil was purified by flash chromatography (eluant AcOEt:hexanes 3:7) to obtain 14.75 g (86% yield) of tan crystals, m.p. 55–56 °C. $[\alpha]_D^{22} = +76$ (c = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): δ =

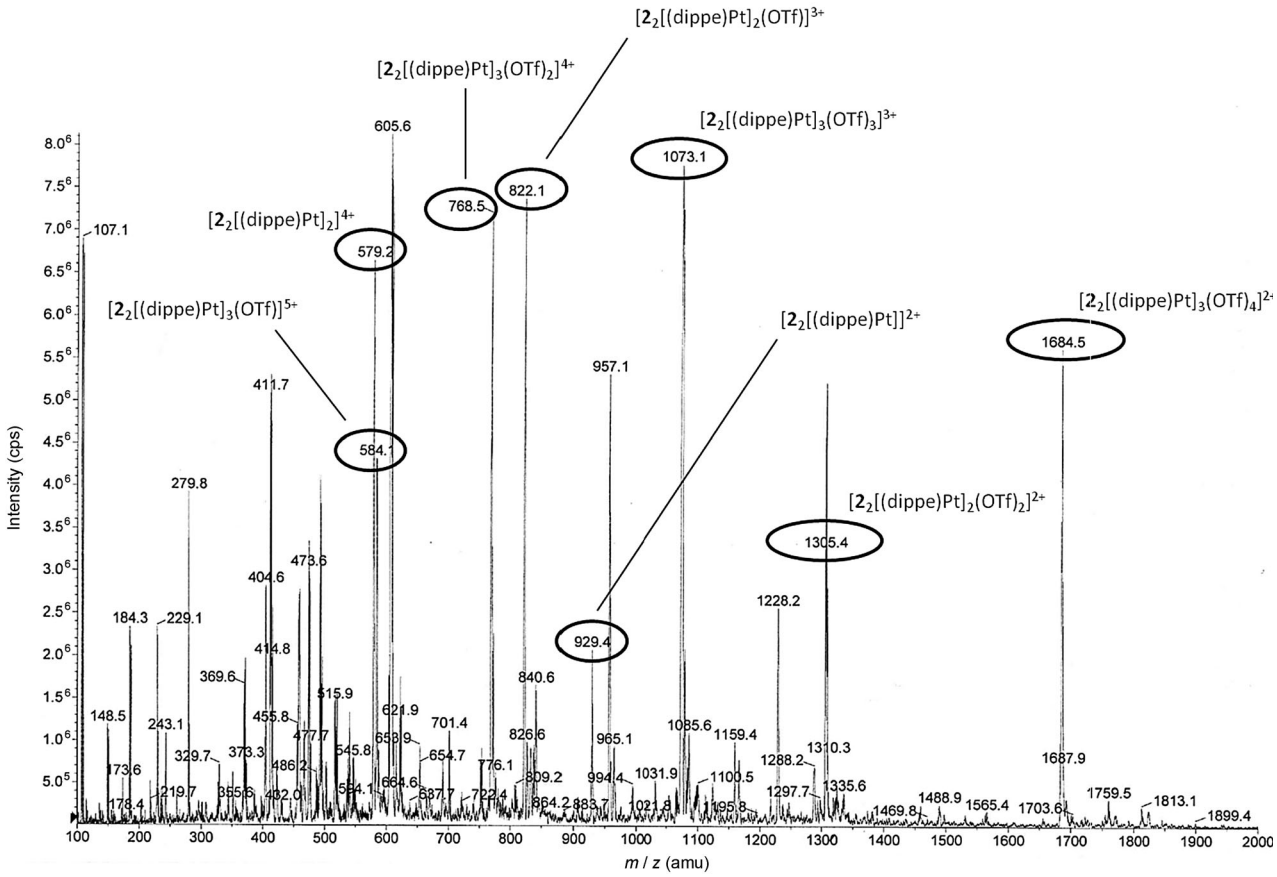


Figure 8. ESI mass spectrum of $[Pt_3(syn\text{-}\mathbf{2})_2(dippe)_3](OTf)_6$.

6.14 (1H, brs), 4.12 (1H, brs), 2.48 (1H, dd, $J=3.8$, 1.0 Hz), 2.40 (1H, ddd, $J=13.2$, 3.8, 0.6 Hz), 1.13 (3H, s), 1.07 (1H, brs), 0.96 (1H, dd, $J=13.2$, 2.5 Hz), 0.95 (3H, s), 0.82 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=143.4$, 100.0, 78.4, 63.4, 61.1, 59.5, 37.6, 20.3, 18.8, 10.2 ppm; IR (KBr): $\tilde{\nu}=3369$, 2957, 1567, 1448, 1287, 1059 cm^{-1}; MS (EI, 70 eV): m/z (%): 234 [$M^+-C_2H_4O$] (53), 151 (57), 109 (52), 107 (100), 105 (54); elemental analysis (%) calcd for $C_{10}H_{15}IO$ (278.13): C 43.18, H 5.44; found: C 42.83, H 5.82.

(1*S*,4*S*)-5-Iodo-1,7,7-trimethylbicyclo[2.2.1]hept-5-en-2-one (10): A mixture of 5-iodo-2-hydroxy-1,7,7-trimethylbicyclo[2.2.1]hept-5-ene (**8**; 18.2 g, 65.5 mmol), *N*-methylmorpholine *N*-oxide (13.0 g, 111 mmol), $RuCl_3{\cdot}H_2O$ (0.44 g, 1.96 mmol, 3 mol% Ru) and activated 4 Å molecular sieves (18 g) in acetonitrile (300 mL) was stirred at room temperature under Ar for 3 h. The mixture was filtered on a Celite pad, the solid washed with CH_2Cl_2 (50 mL) and the filtrate was concentrated at reduced pressure. The residue was diluted in 1 M aqueous HCl (150 mL) and the mixture was extracted with pentane (3×100 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (50 mL), saturated aqueous $Na_2S_2O_5$ (50 mL), saturated aqueous NaCl (50 mL), dried over $MgSO_4$ and concentrated in vacuo. The resulting oil was purified by flash chromatography (eluant Et_2O:*n*-pentane in gradient from 0:10 to 1.5:8.5) to obtain 15.8 g (87% yield) of **10** as pale yellow oil. $[\alpha]_D^{22}=+571$ ($c=$ 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=5.97$ (1H, dd, $J=1.1$, 1.0 Hz), 2.74 (1H, dd, $J=3.5$, 1.1 Hz), 2.18 (1H, ddd, $J=16.9$, 3.5, 1.0 Hz), 1.96 (1H, d, $J=16.9$ Hz), 1.14 (3H, s), 1.04 (3H, s), 0.92 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=213.4$, 139.8, 104.6, 68.2, 60.6, 60.2, 34.8, 19.4, 19.2, 6.6 ppm; IR (film): $\tilde{\nu}=2961$, 1744, 1561, 1023, 673 cm^{-1}; MS (EI, 70 eV): m/z (%): 276 [M^+] (19), 234 (100), 107 (87), 91 (60), 79 (29), 77 (18); elemental analysis (%) calcd for $C_{10}H_{13}IO$ (276.11): C 43.50, H 4.75; found: C 43.18, H 4.56.

General procedure for cyclotrimerization screening (Table 1): An oven-dried Schlenk tube equipped with a magnetic stir bar was charged with ligand (0.05 mmol), Pd source (0.025 mmol), base (2.5 mmol), additives and activated 4 Å molecular sieves (200 mg) and closed with a septum The vessel was evacuated and backfilled with argon three times, and then a degassed solution of anhydrous nBu$_4$NOAc (0.75 g, 2.5 mmol) in 3 mL of dry solvent was added by syringe. The solution was heated to 100 °C for 15 min and then a solution of **10** (138 mg, 0.5 mmol) in 1 mL of solvent was added by syringe. The mixture was stirred at 100 °C for 4 h, cooled to room temperature, diluted in Et_2O and washed with 1 M HCl. A known amount of tetradecane was added to the solution as internal standard and then the reaction mixture was analyzed by GC.

Scaled-up procedure for cyclotrimerization of (10): A mixture of dry KOAc (15.4 g, 147 mmol), dry K_2CO_3, (20.3 g, 147 mmol), activated 4 Å molecular sieves (16 g), $Pd(OAc)_2$ (656 mg, 2.92 mmol) and dppf (1.618 mg, 1.46 mmol) was evacuated and backfilled with argon three times, and then a degassed solution of anhydrous nBu$_4$NOAc (44.3 g, 147 mmol) in 200 mL of freshly distilled toluene was added by syringe. The solution was heated to 100 °C for 30 min (the mixture turned black) and then a solution of **9** (8.10 g, 29.3 mmol) in dry toluene (30 mL) was added by syringe. The mixture was stirred at 100 °C for 14 h, cooled to room temperature and filtered on a Celite pad, and the solid was washed with AcOEt. Water (50 mL) was added to the filtrate and the resulting mixture was extracted with Et_2O (3×50 mL). The combined organic layers were washed with 1 M HCl (2×50 mL) and saturated aqueous $NaHCO_3$ (50 mL), dried over $MgSO_4$ and concentrated at reduced pressure. The residual oil was purified by flash chromatography (eluant Et_2O:cyclohexane in gradient from 1:9 to 5:5).

First eluate: 1,7,7-trimethyl-5-(4,7,7-trimethyl-5-oxobiciclo[2.2.1]hept-2-en-2-yl)bicyclo[2.2.1]hept-5-en-2-one (**11**), recrystallized from cyclohexane, 0.70 g (16% yield) as colourless crystals, m.p. 185 °C. $[\alpha]_D^{22}=+1509$ ($c=1.1$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=5.41$ (1H, s), 2.68 (1H, d, $J=3.1$ Hz), 2.25 (1H, dd, $J=16.7$, 3.1 Hz), 1.63 (1H, d, $J=16.8$ Hz), 1.07 (3H, s), 1.05 (3H, s), 0.92 ppm (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=214.4$, 149.6, 127.3, 66.8, 59.1, 48.9, 36.2, 19.4, 19.1, 6.6 ppm; IR (KBr): $\tilde{\nu}=2962$, 1737, 1442, 1030, 757 cm^{-1}; MS (EI, 70 eV): m/z (%): 298 [M^+] (47), 214 (100), 199 (33), 91 (23); elemental analysis (%) calcd for $C_{20}H_{26}O_2$ (298.42): C 80.50, H 8.78; found: C 80.25, H 8.86.

Second eluate: (+)-*syn*-(1*R*,4*S*,5*R*,8*S*,9*R*,12*S*)-3,4,7,8,11,12-hexahydro-1,5,9,13,13′,14,14′,15,15′-nonamethyl-1,4:5,8:9,12-trimethanotriphenylen-2,6,10-trione (*syn*-**5**), recrystallized from methanol, 2.56 g (59% yield) as colourless crystals, m.p. 272–273 °C. $[\alpha]_D^{22}=+691$ ($c=1.4$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=3.36$ (3H, d, $J=4.0$ Hz), 2.46 (3H, dd, $J=17.6$, 4.0 Hz), 1.80 (3H, d, $J=17.6$ Hz), 1.33 (9H, s), 1.02 (9H, s), 0.85 ppm (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=213.8$, 143.6, 132.6, 65.1, 58.8, 46.1, 38.9, 20.0, 19.2, 8.0 ppm; IR (KBr): $\tilde{\nu}=2966$, 1739, 1038 cm^{-1}; MS (EI, 70 eV): m/z (%): 444 [M^+] (50), 402 (100), 374 (58), 360 (87), 346 (68), 331 (79).

Third eluate: (+)-*anti*-(1*S*,3*R*,4*R*,5*R*,6*R*,8*S*,9*R*,10*R*,12*S*)-1,2,7,8,11,12-hexahydro-4,5,9,13,13′,14,14′,15,15′-nonamethyl-1,4:5,8:9,12-trimethanotriphenylene-3,6,10-trione (*anti*-**5**), 0.48 g (11% yield) as colourless crystals, m.p. 240 °C (decomp). $[\alpha]_D^{22}=+753$ ($c=1.1$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=3.33$ (1H, d, $J=4.0$ Hz), 3.15 (1H, d, $J=3.8$ Hz), 3.08 (1H, d, $J=3.9$ Hz), 2.58 (1H, dd, $J=17.5$, 3.9 Hz), 2.56 (1H, dd, $J=17.4$, 3.8 Hz), 2.46 (1H, dd, $J=17.5$, 3.9 Hz), 2.05 (1H, d, $J=17.4$ Hz), 1.96 (1H, d, $J=17.5$ Hz), 1.90 (1H, d, $J=17.5$ Hz), 1.36 (3H, s), 1.33 (3H, s), 1.32 (3H, s), 1.05 (3H, s), 0.98 (3H, s), 0.96 (3H, s), 0.81 (3H, s), 0.66 (3H, s), 0.59 ppm (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=214.4$, 214.0, 213.5, 145.0, 141.8, 140.0, 138.4, 137.9, 131.9, 66.7, 66.4, 65.4, 60.0, 59.9, 59.5, 59.3, 46.7, 46.3, 45.4, 39.9, 39.6, 39.3, 20.2, 20.14, 20.10, 19.5, 19.38, 19.37, 9.8, 9.8, 8.2 ppm; IR (KBr): $\tilde{\nu}=2970$, 1742, 1392, 1029 cm^{-1}; MS (EI, 70 eV): m/z (%): 444 [M^+] (58), 402 (66), 374 (63), 360 (79), 345 (100), 331 (68), 207 (25); elemental analysis (%) calcd for $C_{30}H_{36}O_3$ (444.61): C 81.04, H 8.16; found: C 80.67, H 8.23.

***syn*-(1*R*,4*R*,5*R*,8*R*,9*R*,12*R*)-2,6,10-Tris(trifluoromethanesulfonate)-4,8,12-hexahydro-1,5,9,13,13′,14,14′,15,15′-nonamethyl-1,4:5,8:9,12-trimethanotriphenylene (*syn*-12)**: KHMDS in toluene (0.5 M, 42.6 mL, 21.3 mmol) was added over 30 min to a solution of *syn*-**5** (2.10 g, 4.73 mmol) in dry THF (50 mL) maintained at −78 °C under Ar, and the mixture was maintained at the same temperature for 2 h. *N*-Phenylbis(trifluoromethanesulfonimide) (7.60 g, 21.3 mmol) in dry THF (20 mL) was added by syringe and the mixture was left to warm to room temperature overnight. The resulting solution was concentrated under vacuum, water (30 mL) was added and the mixture was extracted with Et_2O (3×30 mL). The combined organic extracts were washed with H_2O (30 mL) and saturated aqueous NaCl (30 mL), dried over $MgSO_4$ and concentrated in vacuo. The resulting oil was purified by trituration with MeOH (3×5 mL) to afford the product (3.30 g, 83% yield) as white solid, m.p. 188 °C; $[\alpha]_D^{22}=-26$ ($c=1.1$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=6.18$ (3H, d, $J=3.9$ Hz), 3.63 (3H, d, $J=3.9$ Hz), 1.39 (9H, s), 1.23 (9H, s), 0.76 ppm (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=162.5$, 139.0, 138.6, 122.5, 118.4 (q, $J=321.6$ Hz), 74.1, 60.6, 53.0, 21.5, 19.6, 15.7, 8.5 ppm; IR (KBr): $\tilde{\nu}=$ 2963, 1424, 1143, 1053 cm^{-1}; elemental analysis (%) calcd for $C_{33}H_{33}F_9O_9S_3$ (840.79): C 47.14, H 3.96; found: C 46.79, H 4.23.

***syn*-(1*R*,4*R*,5*R*,8*R*,9*R*,12*R*)-4,8,12-trihydro-1,5,9,13,13′,14,14′,15,15′-nonamethyl-1,4:5,8:9,12-trimethanotriphenylene-2,6,10-tricarbonitrile (*syn*-1)**: TMSCN (0.30 mL, 2.5 mmol) and $[Pd(PPh_3)_4]$ (24 mg, 0.021 mmol) were added to a solution of *syn*-**12** (160 mg, 0.19 mmol) in degassed freshly distilled Et_3N (2 mL) and NMP (0.3 mL) maintained under Ar, and the resulting mixture was heated at 110 °C for 6 h. The cooled solution was partitioned between water (20 mL) and CH_2Cl_2 (3×20 mL), and the combined organic layers were washed with saturated aqueous NaCl (30 mL), dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (eluant CH_2Cl_2:hexane 3:7 to remove phosphorus by-products and AcOEt:hexane 3:7 to obtain the product) to afford *syn*-**1** (70 mg, 78% yield) as a colourless solid, m.p. 310 °C (decomp); $[\alpha]_D^{22}=+440$ ($c=1.1$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.34$ (3H, d, $J=3.5$ Hz), 3.85 (3H, d, $J=3.5$ Hz), 1.55 (9H, s), 1.13 (9H, s), 0.83 ppm (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=155.9$, 140.6, 137.2, 128.3, 115.6, 74.6, 62.6, 56.9, 20.7, 19.4, 10.2 ppm; IR (KBr): $\tilde{\nu}=2975$, 2208, 1466, 1392, 624 cm^{-1}; elemental analysis (%) calcd for $C_{33}H_{33}N_3$ (471.64): C 84.04, H 7.05; found: C 83.69, H 6.72.

***syn*-(1*R*,4*R*,5*R*,8*R*,9*R*,12*R*)-2,6,10-Tris(2-phenylethynyl)-4,8,12-hexahydro-1,5,9,13,13′,14,14′,15,15′-nonamethyl-1,4:5,8:9,12-trimethanotriphenylene (*syn*-13)**: A mixture of $Pd(OAc)_2$ (5.4 mg, 23.8 μmol), PPh_3 (12.6 mg, 47.6 μmol), phenylacetylene (105 μL, 0.95 mmol) and *syn*-**12** (202 mg,

240 μmol) was evacuated and backfilled with argon three times and then degassed freshly distilled toluene (8 mL) and piperidine (0.72 mL, 7.2 mmol) were added by syringe. The mixture was heated at 60 °C for 2 h and after cooling to room temperature it was concentrated in vacuo. The product was purified by silica-gel chromatography (cyclohexane) to give *syn*-**13** (142 mg, 85% yield) as a colourless solid, m.p. 76–78 °C. $[\alpha]_D^{22} = +1119$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.44$–7.37 (6H, series of m), 7.32–7.25 (9H, series of m), 6.67 (3H, d, $J = 3.4$ Hz), 3.73 (3H, d, $J = 3.4$ Hz), 1.51 (9H, s), 1.14 (9H, s), 0.85 ppm (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 144.8$, 139.9, 137.7, 137.3, 131.3, 128.2, 127.8, 123.8, 85.8, 71.9, 62.8, 56.3, 29.7, 21.2, 19.8, 10.7 ppm; IR (KBr): $\tilde{\nu} = 2925$, 2193, 1487, 1384, 755 cm^{-1}; elemental analysis (%) calcd for $C_{54}H_{48}$ (696.96): C 93.06, H 6.94; found: C 92.74, H 6.75.

***syn*-(1*R*,4*R*,5*R*,8*R*,9*R*,12*R*)-2,6,10-Tris(2-ethynyl-4-pyridine)-4,8,12-trihydro-1,5,9,13,13′,14,14′,15,15′-nonamethyl-1,4:5,8:9,12-trimethanotriphenylene (*syn*-2)**: A mixture of $Pd(OAc)_2$ (5.4 mg, 23.8 μmol), PPh_3 (12.6 mg, 47.6 μmol), 4-ethynylpyridine (98 mg, 0.95 mmol) and *syn*-**12** (204 mg, 243 μmol) was evacuated and backfilled with argon three times, and then degassed, freshly distilled toluene (8 mL) and piperidine (0.72 mL, 7.2 mmol) were added by syringe. The mixture was heated at 60 °C for 4 h and after cooling to room temperature it was concentrated in vacuo. The product was purified by flash chromatography on basic alumina (eluant AcOEt:EtOH in gradient from 10:0 to 7:3) to give *syn*-**2** (143 mg, 84% yield) as a pale orange solid, m.p. 140–142 °C. $[\alpha]_D^{22} = +1123$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.56$ (6H, br s), 7.26 (6H, d, $J = 5.3$ Hz), 6.80 (3H, $J = 3.4$ Hz), 3.78 (3H, $J = 3.4$ Hz), 1.52 (9H, s), 1.14 (9H, s), 0.86 ppm (9H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 149.6$, 147.6, 140.2, 137.6, 136.8, 131.8, 125.2, 95.3, 90.4, 72.6, 63.0, 56.5, 21.1, 19.7, 10.6 ppm; IR (KBr): $\tilde{\nu} = 2956$, 2929, 2187, 1599, 1386, 818 cm^{-1}; elemental analysis (%) calcd for $C_{51}H_{45}N_3$ (699.92): C 87.52, H 6.48; found: C 87.41, H 6.46.

(1*S*,4*S*,7*S*)-1,4,7-Triacetonitril-2,2′,5,5′,8,8′-hexamethyl-3,6,9-vinylidenetriindane (3): Methanesulfonyl chloride (155 μL, 2.0 mmol) was added to a solution of *syn*-**5** (200 mg, 0.41 mmol) and pyridine (320 μL, 4.0 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C under Ar atmosphere. The temperature was allowed to rise to room temperature and maintained for 24 h. The resulting solution was concentrated in vacuo, and the residue diluted in water (30 mL) and extracted with Et_2O (3×30 mL). The combined organic extracts were washed with 1 M aqueous HCl (30 mL), H_2O (30 mL) and saturated aqueous NaCl (30 mL), dried over $MgSO_4$ and concentrated in vacuo. The resulting oil was purified by flash chromatography (eluant EtOAc, $R_f = 0.45$) to afford a colourless solid (165 mg, 92% yield), which was recrystallized from CH_2Cl_2:cyclohexane, m.p. = 100–102 °C (decomp). $[\alpha]_D^{22} = +112$ ($c = 1.3$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.38$ (3H, br s), 5.28 (3H, br s), 3.37 (3H, dd, $J = 8.2$ and 2.5 Hz), 2.62 (3H, dd, $J = 17.3$ and 2.5 Hz), 2.42 (3H, dd, $J = 17.3$ and 8.2 Hz), 1.53 (9H, s), 1.18 ppm (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 155.4$, 142.4, 135.4, 118.4, 107.8, 49.7, 47.1, 32.9, 21.6, 19.9 ppm; IR (KBr): $\tilde{\nu} = 2965$, 2927, 2243, 1717, 1638, 1423, 884 cm^{-1}; MS (EI, 70 eV): m/z (%): 435 [M^+] (23), 420 (7), 395 (100), 340 (11); elemental analysis (%) calcd for $C_{30}H_{33}N_3$ (435.60): C 82.72, H 7.64; found: C 82.42, H 7.94.

Titration of *syn*-3 with AgOTf: A 5.75 mM solution of trinitrile **3** in $CDCl_3$ (solution A) and a 390 mM solution of AgOTf in HPLC-grade acetone (solution B) were prepared. Solution A (500 μL) was placed in an NMR tube and solution B was added in portions of 2.8–3.4 μL by microsyringe to a total of 36.6 μL. ^{1}H NMR spectra of solution A and solution A after each addition of solution B were recorded. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.34$ (6H, s), 5.26 (6H, s), 3.38 (6H, t, $J = 3.2$ Hz) 3.28 (6H, dd, $J = 17.6$, 4.4 Hz), 2.92 (6H, dd, $J = 17.4$, 2.8 Hz), 1.37 (18H, s), 1.16 ppm (18H, s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 154.9$, 141.2, 136.0, 120.5, 120.0 (q, $J = 319.6$ Hz), 108.0, 48.2, 45.5, 33.2, 21.5, 19.8 ppm.

Titration of *syn*-1 with AgOTf: A 7.71 mM solution of trinitrile **1** in $CDCl_3$ (solution A) and a 380 mM solution of AgOTf in HPLC-grade acetone (solution B) were prepared. Solution A (500 μL) was placed in an NMR tube and solution B was added in portions of 2.6 μL by microsyringe to a total of 33.8 μL. ^{1}H NMR spectra of solution A and solution A after each addition of solution B were recorded. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.81$ (6H, d, $J = 2.6$ Hz), 3.89 (6H, d, $J = 2.8$ Hz), 1.50 (18H, s), 1.08 (18H, s), 0.80 ppm (18H, s); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 162.3$, 140.8, 136.7, 125.7, 120.2 (q, $J = 319.6$ Hz), 116.6, 74.1, 62.7, 57.3, 20.0, 18.8, 9.5 ppm.

Titration of *syn*-2 with AgOTf: A 3.80 mM solution of tris-pyridine *syn*-**2** in $CDCl_3$ (solution A) and a 380 mM solution of AgOTf in HPLC-grade acetone (solution B) were prepared. Solution A (500 μL) was placed in an NMR tube and solution B was added in portions of 1–1.6 μL with a microsyringe to a total of 16 μL. ^{1}H NMR spectra of solution A and solution A after each addition of solution B were recorded. ^{1}H NMR (300 MHz, [D_6]acetone): $\delta = 8.76$ (12H, d, $J = 6.3$ Hz), 7.64 (12H, d, $J = 6.3$ Hz), 7.02 (6H, d, $J = 3.4$ Hz), 3.94 (6H, d, $J = 3.3$ Hz), 1.59 (18H, s), 1.15 (18H, s), 0.92 ppm (18H, s); ^{13}C NMR (75 MHz, [D_6]acetone): $\delta = 153.5$, 151.6, 142.2, 139.6, 138.4, 136.1, 128.4, 122.8 (q, $J = 320.4$ Hz), 96.1, 94.6, 74.2, 64.9, 58.5, 22.2, 20.7, 11.7 ppm.

Titration of *syn*-2 with [Pt(dppp)(OTf)$_2$]: A 6.00 mM solution of tris-pyridine *syn*-**2** in [D_6]acetone (solution A) and a 50.0 mM solution of [Pt(dppp)]OTf_2 in [D_6]acetone (solution B) were prepared. Solution A (500 μL) was placed in an NMR tube and solution B was added in portions of 10–20 μL with a microsyringe to a total of 140 μL. ^{1}H NMR spectra of solution A and solution A after each addition of solution B were recorded. ^{1}H NMR (300 MHz, [D_6]acetone): $\delta = 8.86$ (12H, d, $J = 5.5$ Hz), 7.73–7.82 (24H, m), 7.39–7.55 (36H, m), 7.08 (12H, d, $J = 5.8$ Hz), 6.97 (6H, d, $J = 3.4$ Hz), 3.86 (6H, d, $J = 3.6$ Hz), 3.41–3.49 (12H, m), 2.25–2.43 (6H, m), 1.48 (18H, s), 1.09 (18H, s), 0.83 ppm (18H, s); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 151.2$, 151.1, 141.6, 138.7, 137.5, 137.0, 134.4 (m), 133.6 (m), 130.8 (m), 130.7, 129.3 (m), 122.1 (q, $J = 318.7$ Hz), 96.6, 94.8, 73.8, 64.4, 58.1, 24.4 (d, $J = 310.7$ Hz), 21.4, 19.8, 18.7 (d, $J = 3.0$ Hz), 11.0 ppm; ^{31}P NMR (122 MHz, CD_3OD): $\delta = -13.9$ ppm, $^1J_{P-Pt} = 3040$ Hz.

Titration of *syn*-2 with [Pt(dippe)(OTf)$_2$]: A 5.50 mM solution of tris-pyridine *syn*-**2** in [D_6]acetone (solution A) and a 50.0 mM solution of [Pt(dippe)$(OTf)_2$] in [D_6]acetone (solution B) were prepared. Solution A (500 μL) was placed in an NMR tube and solution B was added in portions of 10 μL with a microsyringe to a total of 130 μL. ^{1}H NMR spectra of solution A and solution A after each addition of solution B were recorded. ^{1}H NMR (300 MHz, [D_6]acetone): $\delta = 8.88$ (12H, d, $J = 5.5$ Hz), 7.67 (12H, d, $J = 5.8$ Hz), 6.06 (6H, d, $J = 3.4$ Hz), 3.93 (6H, d, $J = 3.6$ Hz), 2.25–2.54 (12H, m), 1.53 (18H, s), 1.30–1.51 (36H, m), 1.13 (18H, s), 0.89–0.97 (12H, m), 0.83 ppm (18H, s); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 152.2$, 151.7, 141.8, 138.8, 138.1, 137.6, 130.4, 121.9 (q, $J = 319.0$ Hz), 97.7, 95.3, 74.3, 64.5, 58.2, 27.1 (d, $J = 34.7$ Hz), 25.0 (d, $J = 33.1$ Hz), 21.4, 21.4 (d, $J = 41.8$ Hz), 20.2, 19.8, 19.7 (d, $J = 30.8$ Hz), 19.2, 18.0, 17.2 (d, $J = 3.2$ Hz), 11.2 ppm; ^{31}P NMR (122 MHz, CD_3OD): $\delta = 65.7$ ppm, $^1J_{P-Pt} = 3129$ Hz.

Mass spectrometry: Mass spectrometric measurements were performed on a API 4000 triple-quadrupole spectrometer (Applied Biosystems/MDS SCIEX, Toronto, Ontario, Canada) equipped with Turbo V source. Mass spectra were acquired in positive-polarity mode. Methanolic solutions (HPLC/MS-grade methanol was purchased from Romil Ltd, Cambridge, UK) with a concentration of 5×10^{-3} M were injected into the ESI source by direct infusion with a syringe pump (Model 11, Harvard Apparatus Inc., Holliston, MA) at 5 μL min^{-1} flow rate. The following tuned conditions were used for silver complexes: curtain gas (CUR): 25 psi; nebulizer gas (GS1): 15 psi; ionization voltage (IS): 5450 V; source temperature (TEM): 50 °C; declustering potential (DP): 80 V; entrance potential (EP): 10 V. For platinum complexes the corresponding parameters were: CUR: 25 psi, GS1: 13 psi; IS: 5500 V; TEM: 20 °C; DP: 76 V; EP: 10 V. Structural identification of ions produced by ESI source was performed by means of MS/MS experiments conducted in product ion scan acquisition mode with a collision energy (CE) of 50 V, collision cell exit potential (CXP) of 15 V and collision gas (CAD) of 6 psi.

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