



# Article Controlling Chiral Self-Sorting in Truxene-Based Self-Assembled Cages

Amina Benchohra<sup>1</sup>, Simon Séjourné<sup>1</sup>, Antoine Labrunie<sup>1</sup>, Liam Miller<sup>1</sup>, Enzo Charbonneau<sup>1</sup>, Vincent Carré<sup>2</sup>, Frédéric Aubriet<sup>2</sup>, Magali Allain<sup>1</sup>, Marc Sallé<sup>1,\*</sup> and Sébastien Goeb<sup>1,\*</sup>

- <sup>1</sup> Laboratoire MOLTECH-Anjou, UMR CNRS 6200, Université d'Angers, SFR MATRIX, 2 Bd Lavoisier, 49045 Angers, France; amina.benchohra@unige.ch (A.B.); simon.sejourne@etud.univ-angers.fr (S.S.); antoine.labrunie@u-paris.fr (A.L.); liam.miller@etu.univ-nantes.fr (L.M.); enzo.charbonneauenzo@etud.univ-angers.fr (E.C.); magali.allain@univ-angers.fr (M.A.)
- <sup>2</sup> LCP-A2MC, FR 2843 Institut Jean Barriol de Chimie et Physique Moléculaires et Biomoléculaires, FR 3624 Réseau National de Spectrométrie de Masse FT-ICR à très haut champ, Université de Lorraine, ICPM, 1 Boulevard Arago, CEDEX 03, 57078 Metz, France; vincent.carre@univ-lorraine.fr (V.C.); frederic.aubriet@univ-lorraine.fr (F.A.)
- \* Correspondence: marc.salle@univ-angers.fr (M.S.); sebastien.goeb@univ-angers.fr (S.G.)

**Abstract:** Coordination driven self-assembly of achiral components, i.e., hexa-alkylated truxene ligands (L) with bis-metallic complexes (M<sub>2</sub>), afforded three chiral face-rotating stereoisomer polyhedra (M<sub>6</sub>L<sub>2</sub>). By tuning the length of the alkyl chains as well as the distance between both ligands facing each other in the self-assemblies (M<sub>6</sub>L<sub>2</sub>), one can control the diastereomeric distribution between the expected homo- and hetero-chiral structures.

Keywords: supramolecular chemistry; self-assembly; self-sorting; metalla-cage; chirality; truxene

# 1. Introduction

The labile nature of the coordination bond has been extensively exploited for the selfassembly, under thermodynamic control, of simple building blocks into sophisticated 2D or 3D architectures [1–3]. The latter can be used to target applications such as molecular recognition, drug delivery, molecular separation or even catalysis in confined spaces [4–14]. In line with the work developed in the field of molecular machines, researchers are particularly interested in designing stimuli-responsive self-assembled structures, whose properties or shape can be tuned through light irradiation, application of a current or addition of a chemical [15–23]. Nevertheless, most of these self-assembled structures are achiral. Developing new synthetic strategies to convert symmetric ligands into chiral self-assemblies is highly desirable since the latter can be in principle useful for enantioselective sensing or asymmetric transformations [24–29]. While the most common synthetic strategy relies on the use of one chiral building block along the self-assembly process [27,30,31], examples in which achiral components are self-sorted [32,33] to form either homochiral [34–41] or heterochiral [34,35,42,43] self-assemblies are also depicted.

In this context,  $C_3$  symmetrical cages have emerged as an interesting class of supramolecular compounds for studying chirality dynamics [44]. Among others, this phenomenon was recently observed with the family of face-rotating polyhedral [45–51]. They are obtained by the combination of chiral or achiral linkers with face-rotating moieties such as triazatruxene [45,46] or truxene [40,48–52] for example. Hexa-alkylated truxene derivatives exhibit a  $C_{3h}$ -symmetry and show both clockwise (C, green) and anti-clockwise (A, blue) faces as defined by the rotation sense of the three sp3 bridges along the  $C_3$  axis (Figure 1a). Functionalization of the latter with three pyridine units allows for producing prochiral ligands able to self-assemble with bis-metallic complexes into  $M_6L_2$  cages (Figure 1b). Upon self-assembling, the ligands lose their mirror symmetry, which results in several possible



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**Copyright:** © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). stereoisomers, i.e., an enantiomers couple (CC/AA) and the meso form (AC). We showed recently that the hexabutyl truxene ligand **LBu** reacts with the hydroxynaphtoquinonato diruthenium complex **Ru** to afford, thanks to a chiral self-sorting process, only the CC/AA enantiomers couple [53]. We hypothesized this selectivity was due to the through space interactions occurring between the butyl chains located within the cavity, which self-organize in an alternated way to minimize the constraints. Herein, we investigate further the role of those interactions while studying other combinations of new hexa-alkyl truxene-based ligands and bis-metallic complexes of various lengths.



**Figure 1.** (a) Hexa-alkylated truxene-based ligand (L) showing two rotational faces (Clockwise (C), green and Anticlockwise (A), blue); and (b) the three possible metalla-cage structures ( $M_6L_2$ ) that can be obtained upon self-assembling with *bis*-metallic complexes.

# 2. Results and Discussion

Ligands **LEt** and **LBu** (Scheme 1) were synthetized from previously described hexaalkyl truxene derivatives **1a** and **1b** respectively [54–56]. After a selective tri-bromination of the truxene moiety using Br<sub>2</sub> that affords compounds **2a** and **2b** (>80% yields), palladocatalysed Suzuki-Miyaura cross-coupling reactions with 4-pyridinylboronic were carried out in a mixture of toluene and ethanol in basic conditions. The target ligands **LEt** and **LBu** were obtained in good yields considering that three sites are functionalized during the reaction (60% and 46%, respectively).

Single crystals of ligand **LEt** were obtained by slow evaporation of its solution in chloroform. The corresponding crystallographic structure is depicted in Figure 2 and compared to the previously described ligand **LBu**. Both ligands show nearly similar structural characteristics with a planar truxene core which places the three peripherical nitrogen atoms in the same plane. To minimize H-H interactions, the pyridine shows an average rotation angle of  $38.6(1)^{\circ}$  (**LEt**) and  $40.8(1)^{\circ}$  (**LBu**) with the central truxene core [57]. In accordance with the C<sub>3</sub> symmetry of both ligands, an angle of  $120^{\circ}$  is measured between each pyridine axis. Finally, the n-alkyl chains are arranged on both opposite sides, almost perpendicularly to the truxene plane.



**Scheme 1.** Synthesis of ligands **LEt** and **LBu**, and metalla-cages **BuRu**, **EtRu** and **BuRh**, as well as their respective stereoisomeric ratio.



**Figure 2.** X-Ray crystal structures of **LEt** (left) and **LBu** (right): (**a**,**c**) top views (clockwise face in green); and (**b**,**d**) lateral views showing both rotating faces (clockwise in green, anticlockwise in blue).

The self-assembly reactions were proceeded between two equivalents of ligands and three equivalents of bis-metallic complexes, with the objective of forming  $M_6L_2$  cages which associate two truxene entities face to face (Scheme 1). The resulting cavity is thus intended to be filled by the n-alkyl groups which are intercalated between the two aromatic platforms. Our previous work showed the importance of through space interactions between n-alkyl chains to drive the relative spatial organization of the ligands within the self-assembly. With the aim of controlling the ratio between AA/CC and AC species, we studied new ligand-complex combinations, i.e., LEt with Ru and LBu with Rh. Based on the X-ray structures of LEt and LBu, we extracted the distance "a" between the sp<sup>3</sup> carbon of the Ar-Ar bridge in the truxene moiety and the sp<sup>3</sup> carbon of the terminal methyl group of the

alkyl chain (Figure 2). On the other hand, "b" is defined as the intermetallic distance within the **Ru** and **Rh** bimetallic complexes as extracted from literature data. From these values, we calculated "c" (= b - 2a) which reflects the minimal distance between terminal methyl groups of opposite dangling alkyl chains as function of the dinuclear bridge (Table 1). While this value is negative (c = -1.6 Å) for **BuRu** cage, for which only the CC and AA enantiomers are observed, it increases to 2.9 Å for **BuRh**, meaning the alkyl chains are too far away to interact in this case. The situation for **EtRu** appears intermediate.

Table 1. a, b and c values within the self-assembled structures BuRu, EtRu and BuRh.

	Alkyl Chain Length a (Å)	Metal-Metal Distance b (Å)	c = b - 2a (Å)
BuRu	5.0	8.4	-1.6
EtRu	2.6	8.4	2.2
BuRh	5.0	12.9	2.9

All reactions were carried out in methanol- $d_4$  at  $C = 10^{-3}$  M and well-resolved <sup>1</sup>H NMR spectra, suggesting the formation of one discrete species, were observed in the three cases after 4 h at 50 °C (Figures S7, S10 and S14). The corresponding cages **BuRu**, **EtRu** and **BuRh** were isolated by precipitation with diethyl ether in ca. 80% yield. ESI-FTICR-HRMS spectrometry experiments were carried out in methanol at  $C = 10^{-4}$  M on each sample (Figure 3). These measurements confirm the expected M<sub>6</sub>L<sub>2</sub> stoichiometry in the three cases, with characteristic multi-charged isotopic patterns localized at m/z = 789.65155, 1024.30257 and 1415.38762 for compound **BuRu** (main contributions, Figure S17), at m/z = 721.97871, 939.71148 and 1302.59947 for **EtRu** (main contributions, Figure S18) and at m/z = 735.20408, 882.73054, 1089.06712 and 1398.57199 for **BuRh** (main contributions, Figure S19).



**Figure 3.** ESI-FTICR mass spectra recorded in methanol ( $C = 10^{-4}$  M) of: (**a**) **BuRu**; (**b**) **EtRu**; and (**c**) **BuRh**.

The <sup>1</sup>H NMR, <sup>1</sup>H COSY NMR and <sup>1</sup>H DOSY NMR spectra of the three cages are shown in Figure 4 (high-field region) and Figures S7–S16. The diffusion measurements revealed in each case one single diffusion value (D). **BuRu** and **EtRu** self-assemblies exhibit a similar diffusion coefficient close to  $3.0 \times 10^{-10}$  m<sup>2</sup>·s<sup>-1</sup> while this value decreases for **BuRh** cage (D =  $2.3 \times 10^{-10}$  m<sup>2</sup>·s<sup>-1</sup>), as expected for a larger edifice. Hydrodynamic radii of ca. 13 Å and 17 Å were calculated from the Stokes-Einstein equation [58], in agreement with the



formation of  $M_6L_2$  species. The case of **BuRu** was deeply investigated in a previous work, establishing the exclusive formation of the  $D_3$  symmetric **CC** and **AA** enantiomers [53].

**Figure 4.** <sup>1</sup>H NMR (298 K,  $C = 10^{-3}$  M, high-field region) of: (a) ligand **LBu** in CDCl<sub>3</sub>; (b) ligand **LEt** in CDCl<sub>3</sub>; (c) **BuRu** in methanol-d<sub>4</sub> after 12 h; (d) **EtRu** in methanol-d<sub>4</sub> after 4 h; and (e) **BuRh** in methanol-d<sub>4</sub> after 12 h and (d') **EtRu** in methanol-d<sub>4</sub> after 12 h. The following nomenclature has been used: protons 4 correspond to terminal CH<sub>3</sub> from butyl chains and protons 2 correspond to terminal CH<sub>3</sub> from ethyl chains; grey and black assignments correspond to inner and outer cavity protons respectively; i and ii denote the proper signatures of the AA/CC enantiomers and the AC meso derivative respectively; 1 and 2 are used to differentiate the diastereotopic aliphatic protons (SI).

This was assigned to through-space van der Waals interaction between butyl chains facing each other inside the cavity (c = -1.6 Å). While in this case only one set of signals for the truxene backbone (Figure S7, protons  $\alpha$ ,  $\beta$ ,  $\alpha$ , b and c) and for methyl groups from the alkyl chains is observed, these signals are splitted in the cases of **EtRu** (Figures S10, S11 and 4d,d') and **BuRh** (Figures S14 and 4e), suggesting the presence of the mixture of diastereoisomers. The relative integrals of protons 4 (**BuRu** and **BuRh**) and protons 2 (**EtRu**) were used to determine the proportion of enantiomers AA/CC vs. the meso form AC. On this basis, a 50/50 statistical mixture of the diastereoisomers is determined for **BuRh** (Figure 4e), which confirms the absence of interaction between both opposite faces in the structure (c = 2.9 Å). A similar ratio is observed for **EtRu** at short reaction time (Figure 4d) but the latter evolves to 66/33 after several hours (Figure 4d'). This indicates that the reaction is thermodynamically driven and confirms the crucial role of the interligand interactions inside the cavity. Regarding (i) the evolution of the ratio over time, (ii) the selectivity observed for **BuRu** and (iii) the statistical mixture observed for **BuRh**, the dominant species in **EtRu** should be the couple of enantiomers AA/CC.

Single crystals were obtained for self-assemblies **BuRu** and **BuRh** from slow diffusion of methyl *tert*-butyl ether in their methanolic solutions (Figure 5). The **BuRu** cage crystallized in the non-centrosymmetric P3<sub>1</sub>21 space group with a Flack parameter of 0.44 indicating enantio-enriched crystal (enriched in AA) and the **BuRh** cage in the centrosymmetric C 2/c space group. Interestingly, if **BuRh** solution speciation revealed a statistical mixture of all stereoisomers, only AA/CC enantiomeric pair was observed in the crystalline phase. Despite numerous attempts, no single crystals of **EtRu** suitable for XRD measurements could be obtained. We have therefore modeled the corresponding compound by MM+ calculations using the **CC-BuRu** structure as a starting-point. Unlike topologically similar metalla-structures in which a large tilt of the bis-ruthenium complexes allows the facing ligands planes to be closer in order to maximize the  $\pi$ - $\pi$  interactions [59,60], the alkyl chains present inside the cavity of **BuRu**, **EtRu** and **BuRh** strongly limits structural devia-

tion from right prismatic geometry and maintain both truxene moieties at distances close to the intermetallic one. These are however slightly shorter than the M-M distances. As a result, the trigonal prisms are only slightly distorted with average Bailar angles ranging from 7.9° to 16° (Figure S20). Moreover, in each case, the pyridyl rings are tilted by ca. 20° out of the plane of the truxene moiety. All these parameters generate two types of chirality, a double rosette (M/P) and a propeller isomerism ( $\Delta/\Lambda$ ). Both are dependent one other in these structures since only the enantiomers (AA, M,  $\Delta$ ) and (CC, P,  $\Lambda$ ) are observed [60,61].



**Figure 5.** X-ray crystal structures of: (a) **BuRu**; (c) **BuRh** and MM+ simulation of (b) **EtRu** (only CC forms are represented). Schematic representation of chirality elements (d).

# 3. Materials and Methods

## 3.1. Chemicals

Compounds **1b** [56], **2b** and **LBu** [53], as well as compounds **1a** and **2a** [62], and complexes **Ru** [63] and **Rh** [64] were synthesized using procedures described in the literature. All reagents were of commercial reagent grade and were used without further purification. Silica gel chromatography was performed with a SIGMA Aldrich Chemistry SiO<sub>2</sub> (pore size 60 Å, 40–63 µm technical grades).

# 3.2. Instrumentation

Characterizations and NMR experiments were carried out on a NMR Bruker Avance III 300 spectrometer at 298 K, using perdeuterated solvents. <sup>1</sup>H DOSY NMR spectra were analyzed with MestReNova software. MALDI-TOF-MS spectra were recorded on a MALDI- TOF Bruker Biflex III instrument using a positive-ion mode. ESI-FTICR mass spectra at very high resolution were performed in positive detection mode on a 7T Solarix 2xR (Bruker Daltonics, Marne la Vallée, France).

## 3.3. Experimental Procedure and Characterization Data

# 3.3.1. Ligand LEt

To a stirred solution of **2a** (0.50 g, 0.669 mmol) in toluene (25 mL) and EtOH (12 mL) was added 4-pyridine boronic acid (0.33 g, 2.68 mmol, 4 equivalents) at room temperature. Then K<sub>2</sub>CO<sub>3</sub> (1.94 g, 14.05 mmol, 21 equivalents) in water (8 mL) was added to the solution at room temperature. The solution was degassed with argon for 40 min at room temperature. Pd(PPh<sub>3</sub>)<sub>4</sub> (0.23 g, 30%) was then added to the solution. The solution was stirred at 90 °C. After 64 h, the mixture was cooled to room temperature and extracted with dichloromethane. The organic extracts were washed with water, dried over magnesium sulfate and the solvent were evaporated. The residue was purified by chromatography on silica gel using ethyl acetate/dichloromethane/methanol/triethylamine (from 75/25/0/0 to 42/42/15/1) as an eluant to give ligand LEt as a yellow powder (369 mg, 74%). <sup>1</sup>H NMR (300 MHz, 298 K, CDCl<sub>3</sub>):  $\delta$  8.74–8.72 (m, 6H), 8.50–8.47 (d, <sup>3</sup>*J* = 8.9 Hz, 3H), 7.76 (s, 3H), 7.75 (d, <sup>3</sup>*J* = 7.1 Hz, 3H), 7.68–7.65 (m, 6H), 3.12–3.05 (m, 6H), 2.31–2.17 (m, 6H), 0.29 (t, <sup>3</sup>*J* = 7.1 Hz, 18H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>):  $\delta$  153.85, 150.43, 148.23, 145.27, 141.45, 138.50, 136.52, 125.45, 125.20, 121.56, 120.67, 57.18, 29.65, 8.65. HRMS (MALDI-TOF): found: 741.4110; Calculated: 741.4083.

# 3.3.2. Self-Assembly EtRu

A mixture of **LEt** (10.00 mg, 13.5 µmol, 2 equiv.) and complex **Ru** (19.35 mg, 20.0 µmol, 3 equiv.) in methanol (2 mL) was stirred 20 h at 50 °C. Then, diethyl ether (5 mL) was added and the resulting suspension was centrifuged. The resulting solid was washed twice with diethyl ether to give **EtRu** (24.02 mg, 4.5 µmol, 83%) as a dark solid. <sup>1</sup>H NMR (300 MHz, MeOD):  $\delta$  8.50–8.46 (m, 12H), 8.32–8.26 (m, 6H), 7.90–7.77 (m, 24H), 7.32–7.31 (m, 12H), 5.92–5.88 (m, 12H), 5.69–5.65 (m, 12H), 2.92–2.88 (m, 12H), 2.70–2.50 (m, 6H), 2.17–2.16 (m, 24H), 2.02–1.95 (m, 6H), 1.37 (d, <sup>3</sup>*J* = 6.9 Hz, 36H), 0.10–(-0.02) (m, 18H), -0.32–(-0.49) (m, 18H). <sup>1</sup>H DOSY NMR (300 MHz, MeOD) D =  $3.03 \times 10^{-10}$  m<sup>2</sup>·s<sup>-1</sup>. FTICR-HRMS (*m*/*z*), **[EtRu** – 3TfO<sup>-</sup>]<sup>3+</sup>: found: 1302.59965, calculated 1302.59947, **[EtRu** – 4TfO<sup>-</sup>]<sup>4+</sup>: found: 939.71154, calculated 939.71148, **[EtRu** – 5TfO<sup>-</sup>]<sup>5+</sup>: found: 721.97871, calculated 72197870.

# 3.3.3. Self-Assembly BuRh

A mixture of **LBu** (10.00 mg, 10.6 µmol, 2 equiv.) and complex **Rh** (23.98 mg, 15.9 µmol, 3 equiv.) in methanol (2.5 mL) was stirred 1 h at 50 °C. Then, diethyl ether (5 mL) was added and the resulting suspension was centrifuged. The resulting solid was washed twice with diethyl ether to give **BuRh** (25.14 mg, 3.92 µmol, 74%) as a yellow solid. <sup>1</sup>H NMR (300 MHz, 298 K, MeOD):  $\delta$  10.38–10.35 (m, 12H), 9.93 (d, <sup>3</sup>*J* = 7.3 Hz, 12H), 8.72–8.68 (m, 12H), 8.47–8.43 (m, 12H), 8.33–8.30 (m 6H), 7.95–7.75 (m, 24H), 2.90–2.86 (m, 6H), 2.71–2.67 (m 6H), 2.13–2.08 (m, 6H), 1.95–1.82 (m, 96H), 0.95–0.87 (12H), 0.50–0.05 (m, 42H), -0.06–(-0.20) (m, 12H), -0.36 (t, <sup>3</sup>*J* = 7.2Hz), -0.44 (t, <sup>3</sup>*J* = 7.3 Hz, 9H). <sup>1</sup>H DOSY NMR (300 MHz, MeOD): D = 2.34 × 10<sup>-10</sup> m<sup>2</sup>·s<sup>-1</sup>. FTICR-HRMS (*m*/*z*): [**BuRh** – 4OTf<sup>-</sup>]<sup>4+</sup>: found: 1398.57256; calculated 1398.57199, [**BuRh** – 5Otf<sup>-</sup>]<sup>5+</sup>: found: 1089.06707; calculated 1089.06712, [**BuRh** – 6Otf<sup>-</sup>]<sup>6+</sup>: found: 882.72998; calculated: 882.73054, [**BuRh** – 7Otf<sup>-</sup>]<sup>7+</sup>: found: 735.20397; calculated: 735.20408.

## 3.4. Molecular Modelling

Molecular modelling was performed by using the molecular mechanics force field MM+ method from the HyperChem 8.0.3 program (Hypercube, Inc., Waterloo, ON, Canada,) configured in vacuo, with a RMS of  $10^{-5}$  kcal/mole, a number of maximum cycles of 32,500, and a Polak-Ribiere algorithm. Counter anions were omitted to simplify the calculation.

## 3.5. X-ray Crystallographic Analysis

X-ray single-crystal diffraction data were collected at low temperature on a Rigaku Oxford Diffraction SuperNova diffractometer equipped with Atlas CCD detector and microfocus Cu-K $\alpha$  radiation ( $\lambda$  = 1.54184 Å). The structures were solved by dual-space algorithm, expanded and refined on F<sup>2</sup> by full matrix least-squares techniques using SHELX programs (G. M. Sheldrick, SHELXT 2018/2 and SHELXL 2018/3). All non-H atoms were refined anisotropically and multiscan empirical absorption was corrected using CrysAlisPro program (CrysAlisPro 1.171.40.45a and 1.171.41.118a, Rigaku Oxford Diffraction, 2019–2021). The H atoms were placed at calculated positions and refined using a riding model.

The structure refinement of **BuRh** showed disordered electron density which could not be reliably modeled. The program PLATON/SQUEEZE was used to add the corresponding scattering contribution to the calculated structure factors. This electron density can be attributed to solvent molecules (methyl tert-butyl ether (MTBE)) and missing triflate molecules (48 CF<sub>3</sub>SO<sub>3</sub> anions). The assumed solvent composition and missing anions were included in the calculation of the empirical formula, formula weight, density, linear absorption coefficient, and F(000).

Crystallographic data for LEt:  $C_{54}H_{51}N_3$ , M = 741.97, T = 200K, colorless prism,  $0.243 \times 0.137 \times 0.108 \text{ mm}^3$ , monoclinic, space group *Cc*, a = 16.8429(4) Å, b = 29.2254(7) Å, c = 8.8287(3) Å,  $\beta$  = 104.094(3)°, V = 4215.0(2) Å3, Z = 4,  $\rho$ calc = 1.169 g/cm<sup>3</sup>,  $\mu$  = 0.513 mm<sup>-1</sup>, F(000) = 1584,  $\theta$ min = 3.024°,  $\theta$ max = 72.419°, 15675 reflections collected, 6363 unique (Rint = 0.0661), parameters/restraints = 520/2, R1 = 0.0631 and wR2 = 0.1739 using 5960 reflections with I > 2\sigma(I), R1 = 0.0657 and wR2 = 0.1786 using all data, GOF = 1.047, -0.300 <  $\Delta\rho$  < 0.237 e.Å-3. CCDC 2183860.

Crystallographic data for **BuRh**:  $C_{376}H_{516}F_{36}N_{24}O_{56}Rh_6S_{12}$ , M = 7954.28, T = 150K, yellow prism,  $0.13 \times 0.076 \times 0.027 \text{ mm}^3$ , monoclinic, space group C2/*c*, a = 39.414(3) Å, b = 24.8816(17) Å, c = 40.900(6) Å,  $\beta$  = 98.08(1)°, V = 39711(7) Å3, Z = 4, pcalc = 1.330 g/cm<sup>3</sup>,  $\mu$  = 3.291 mm<sup>-1</sup>, F(000) = 16696,  $\theta$ min = 2.916°,  $\theta$ max = 73.304°, 85378 reflections collected, 37770 unique (Rint = 0.1374), parameters/restraints = 1315/28, R1 = 0.1173 and wR2 = 0.3152 using 10726 reflections with I > 2\sigma(I), R1 = 0.2119 and wR2 = 0.3999 using all data, GOF = 0.927, -0.739 <  $\Delta \rho$  < 0.594 e.Å-3. CCDC 2183861.

## 4. Conclusions

In summary, we synthetized a series of three chiral  $M_6L_2$  metalla-cages from prochiral hexa-alkylated truxene ligands and achiral dinuclear metallic complexes. Remarkably, the diastereomeric ratio between enantiomers AA/CC and the meso AC form can be tuned thanks to the non-covalent interactions occurring between the internal alkyl chains upheld by two opposite facing ligands. While only the AA/CC enantiomers couple is observed in solution in the case of **BuRu**, the metalla-cage **BuRh** exists as the statistical mixture of the three possible stereoisomers. The latter are also observed for **EtRu** through preferentially producing the enantioenriched AA/CC forms. These results unambiguously confirm the crucial role of inter-ligand communication through the alkyl chains in the self-sorting process. Work is under progress to evaluate the binding abilities of these  $M_6L_2$  chiral cages.

**Supplementary Materials:** The following supporting information can be downloaded at: https: //www.mdpi.com/article/10.3390/inorganics10070103/s1, NMR spectra, cif files and check cif files of **LEt**, **EtRu** and **BuRh**.

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#### References

- 1. Sun, Y.; Chen, C.; Liu, J.; Stang, P.J. Recent developments in the construction and applications of platinum-based metallacycles and metallacages via coordination. *Chem. Soc. Rev.* 2020, *49*, 3889–3919. [CrossRef]
- Debata, N.B.; Tripathy, D.; Sahoo, H.S. Development of coordination driven self-assembled discrete spherical ensembles. *Coord. Chem. Rev.* 2019, 387, 273–298. [CrossRef]
- Cook, T.R.; Stang, P.J. Recent Developments in the Preparation and Chemistry of Metallacycles and Metallacages via Coordination. *Chem. Rev.* 2015, 115, 7001–7045. [CrossRef] [PubMed]
- Zhang, D.; Ronson, T.K.; Zou, Y.-Q.; Nitschke, J.R. Metal–organic cages for molecular separations—Nature Reviews Chemistry. Nat. Rev. Chem. 2021, 5, 168–182. [CrossRef]
- 5. Grommet, A.B.; Feller, M.; Klajn, R. Chemical reactivity under nanoconfinement. Nat. Nanotechnol. 2020, 15, 256–271. [CrossRef]
- Percástegui, E.G.; Ronson, T.K.; Nitschke, J.R. Design and Applications of Water-Soluble Coordination Cages. *Chem. Rev.* 2020, 120, 13480–13544. [CrossRef] [PubMed]
- 7. Yadav, S.; Kannan, P.; Qiu, G. Cavity-based applications of metallo-supramolecular coordination cages (MSCCs). *Org. Chem. Front.* **2020**, *7*, 2842–2872. [CrossRef]
- 8. Fang, Y.; Powell, J.A.; Li, E.; Wang, Q.; Perry, Z.; Kirchon, A.; Yang, X.; Xiao, Z.; Zhu, C.; Zhang, L.; et al. Catalytic reactions within the cavity of coordination cages. *Chem. Soc. Rev.* **2019**, *48*, 4707–4730. [CrossRef]
- 9. Gao, W.-X.; Zhang, H.-N.; Jin, G.-X. Supramolecular catalysis based on discrete heterometallic coordination-driven metallacycles and metallacages. *Coord. Chem. Rev.* 2019, 386, 69–84. [CrossRef]
- 10. Rizzuto, F.J.; von Krbek, L.K.S.; Nitschke, J.R. Strategies for binding multiple guests in metal–organic cages. *Nat. Rev. Chem.* **2019**, *3*, 204–222. [CrossRef]
- 11. Zhao, L.; Jing, X.; Li, X.; Guo, X.; Zeng, L.; He, C.; Duan, C. Catalytic properties of chemical transformation within the confined pockets of Werner-type capsules. *Coord. Chem. Rev.* 2019, *378*, 151–187. [CrossRef]
- Casini, A.; Woods, B.; Wenzel, M. The Promise of Self-Assembled 3D Supramolecular Coordination Complexes for Biomedical Applications. *Inorg. Chem.* 2017, 56, 14715–14729. [CrossRef] [PubMed]
- 13. Zarra, S.; Wood, D.M.; Roberts, D.A.; Nitschke, J.R. Molecular containers in complex chemical systems. *Chem. Soc. Rev.* 2015, 44, 419–432. [CrossRef]
- 14. Amouri, H.; Desmarets, C.; Moussa, J. Confined Nanospaces in Metallocages: Guest Molecules, Weakly Encapsulated Anions, and Catalyst Sequestration. *Chem. Rev.* 2012, *112*, 2015–2041. [CrossRef]
- 15. Cai, K.; Zhang, L.; Astumian, R.D.; Stoddart, J.F. Radical-pairing-induced molecular assembly and motion. *Nat. Rev. Chem.* **2021**, *5*, 447–465. [CrossRef]
- 16. Goeb, S.; Sallé, M. Electron-rich Coordination Receptors Based on Tetrathiafulvalene Derivatives: Controlling the Host-Guest Binding. *Acc. Chem. Res.* 2021, *54*, 1043–1055. [CrossRef]
- 17. Wezenberg, S.J. Light-switchable Metal-Organic Cages. Chem. Lett. 2020, 49, 609–615. [CrossRef]
- 18. Chen, L.-J.; Yang, H.-B. Construction of Stimuli-Responsive Functional Materials via Hierarchical Self-Assembly Involving Coordination Interactions. *Acc. Chem. Res.* 2018, *51*, 2699–2710. [CrossRef]
- 19. Kim, T.Y.; Vasdev, R.A.S.; Preston, D.; Crowley, J.D. Strategies for Reversible Guest Uptake and Release from Metallosupramolecular Architectures. *Chem. Eur. J.* 2018, 24, 14878–14890. [CrossRef]
- Zhang, D.; Ronson, T.K.; Nitschke, J.R. Functional Capsules via Subcomponent Self-Assembly. Acc. Chem. Res. 2018, 51, 2423–2436. [CrossRef]
- 21. Diaz-Moscoso, A.; Ballester, P. Light-responsive molecular containers. Chem. Commun. 2017, 53, 4635–4652. [CrossRef] [PubMed]
- 22. Wang, W.; Wang, Y.-X.; Yang, H.-B. Supramolecular transformations within discrete coordination-driven supramolecular architectures. *Chem. Soc. Rev.* 2016, 45, 2656–2693. [CrossRef] [PubMed]
- Qu, D.-H.; Wang, Q.-C.; Zhang, Q.-W.; Ma, X.; Tian, H. Photoresponsive Host–Guest Functional Systems. *Chem. Rev.* 2015, 115, 7543–7588. [CrossRef]
- Trapp, O. Self-amplification of Enantioselectivity in Asymmetric Catalysis by Supramolecular Recognition and Stereodynamics. In Supramolecular Catalysis: New Directions and Developments; van Leeuwen, P.W.N.M., Raynal, M., Eds.; WILEY-VCH: Weinheim, Germany, 2022.

- 25. Zhang, L.; Liu, H.; Yuan, G.; Han, Y.-F. Chiral Coordination Metallacycles/Metallacages for Enantioselective Recognition and Separation. *Chin. J. Chem.* 2021, *39*, 2273–2286. [CrossRef]
- Zhang, J.H.; Xie, S.M.; Zi, M.; Yuan, L.M. Recent advances of application of porous molecular cages for enantioselective recognition and separation. J. Sep. Sci. 2020, 43, 134–149. [CrossRef]
- Pan, M.; Wu, K.; Zhang, J.-H.; Su, C.-Y. Chiral metal–organic cages/containers (MOCs): From structural and stereochemical design to applications. *Coord. Chem. Rev.* 2019, 378, 333–349. [CrossRef]
- Tan, C.; Chu, D.; Tang, X.; Liu, Y.; Xuan, W.; Cui, Y. Supramolecular Coordination Cages for Asymmetric Catalysis. *Chem. Eur. J.* 2019, 25, 662–672. [CrossRef]
- 29. Li, X.; Wu, J.; He, C.; Meng, Q.; Duan, C. Asymmetric Catalysis within the Chiral Confined Space of Metal-Organic Architectures. *Small* **2019**, *15*, e1804770. [CrossRef]
- 30. Chen, L.-J.; Yang, H.-B.; Shionoya, M. Chiral metallosupramolecular architectures. Chem. Soc. Rev. 2017, 46, 2555–2576. [CrossRef]
- 31. Liu, M.; Zhang, L.; Wang, T. Supramolecular Chirality in Self-Assembled Systems. Chem. Rev. 2015, 115, 7304–7397. [CrossRef]
- 32. Li, C.L.; Zuo, Y.; Zhao, Y.Q.; Zhang, S.D. Chiral Self-sorting in Cage-like Compounds. Chem. Lett. 2020, 49, 1356–1366. [CrossRef]
- Jędrzejewska, H.; Szumna, A. Making a Right or Left Choice: Chiral Self-Sorting as a Tool for the Formation of Discrete Complex Structures. Chem. Rev. 2017, 117, 4863–4899. [CrossRef] [PubMed]
- Schulte, T.R.; Holstein, J.J.; Clever, G.H. Chiral Self-Discrimination and Guest Recognition in Helicene-Based Coordination Cages. Angew. Chem. Int. Ed. 2019, 58, 5562–5566. [CrossRef]
- 35. Beaudoin, D.; Rominger, F.; Mastalerz, M. Chiral Self-Sorting of [2+3] Salicylimine Cage Compounds. *Angew. Chem. Int. Ed.* 2017, 56, 1244–1248. [CrossRef]
- Rota Martir, D.; Escudero, D.; Jacquemin, D.; Cordes, D.B.; Slawin, A.M.Z.; Fruchtl, H.A.; Warriner, S.L.; Zysman-Colman, E. Homochiral Emissive Λ8- and Δ8-[Ir8Pd4]16+ Supramolecular Cages. *Chem. Eur. J.* 2017, 23, 14358–14366. [CrossRef]
- Boer, S.A.; Turner, D.R. Self-selecting homochiral quadruple-stranded helicates and control of supramolecular chirality. *Chem. Commun.* 2015, *51*, 17375–17378. [CrossRef]
- Maeda, C.; Kamada, T.; Aratani, N.; Osuka, A. Chiral self-discriminative self-assembling of meso–meso linked diporphyrins. *Coord. Chem. Rev.* 2007, 251, 2743–2752. [CrossRef]
- 39. Lützen, A.; Hapke, M.; Griep-Raming, J.; Haase, D.; Saak, W. Synthesis and Stereoselective Self-Assembly of Double- and Triple-Stranded Helicates. *Angew. Chem. Int. Ed.* **2002**, *41*, 2086–2089. [CrossRef]
- Xu, C.; Lin, Q.; Shan, C.; Han, X.; Wang, H.; Wang, H.; Zhang, W.; Chen, Z.; Guo, C.; Xie, Y.; et al. Metallo-Supramolecular Octahedral Cages with Three Types of Chirality towards Spontaneous Resolution. *Angew. Chem.* 2022, 134, e202203099. [CrossRef]
- 41. Masood, M.A.; Enemark, E.J.; Stack, T.D.P. Ligand Self-Recognition in the Self-Assembly of a [{Cu(L)}2]2+ Complex: The Role of Chirality. *Angew. Chem. Int. Ed.* **1998**, *37*, 928–932. [CrossRef]
- Arribas, C.S.; Wendt, O.F.; Sundin, A.P.; Carling, C.-J.; Wang, R.; Lemieux, R.P.; Wärnmark, K. Formation of an heterochiral supramolecular cage by diastereomer self-discrimination: Fluorescence enhancement and C<sub>60</sub> sensing. *Chem. Commun.* 2010, 46, 4381–4383. [CrossRef] [PubMed]
- 43. Weilandt, T.; Kiehne, U.; Schnakenburg, G.; Lützen, A. Diastereoselective self-assembly of dinuclear heterochiral metallosupramolecular rhombs in a self-discriminating process. *Chem. Commun.* **2009**, *17*, 2320–2322. [CrossRef] [PubMed]
- Qiu, G.; Nava, P.; Colomban, C.; Martinez, A. Control and Transfer of Chirality Within Well-Defined Tripodal Supramolecular Cages. Front. Chem. 2020, 8, 599893. [CrossRef] [PubMed]
- 45. Zhang, D.; Ronson, T.K.; Greenfield, J.L.; Brotin, T.; Berthault, P.; Léonce, E.; Zhu, J.-L.; Xu, L.; Nitschke, J.R. Enantiopure [Cs<sup>+</sup>/Xe⊂Cryptophane]⊂FeII<sub>4</sub>L<sub>4</sub> Hierarchical Superstructures. *J. Am. Chem. Soc.* **2019**, *141*, 8339–8345. [CrossRef] [PubMed]
- Zhang, P.; Wang, X.; Xuan, W.; Peng, P.; Li, Z.; Lu, R.; Wu, S.; Tian, Z.; Cao, X. Chiral separation and characterization of triazatruxene-based face-rotating polyhedra: The role of non-covalent facial interactions. *Chem. Commun.* 2018, 54, 4685–4688. [CrossRef]
- 47. Qu, H.; Tang, X.; Wang, X.; Li, Z.; Huang, Z.; Zhang, H.; Tian, Z.; Cao, X. Chiral molecular face-rotating sandwich structures constructed through restricting the phenyl flipping of tetraphenylethylene. *Chem. Sci.* **2018**, *9*, 8814–8818. [CrossRef]
- Wang, Y.; Fang, H.; Tranca, I.; Qu, H.; Wang, X.; Markvoort, A.J.; Tian, Z.; Cao, X. Elucidation of the origin of chiral amplification in discrete molecular polyhedra. *Nat. Commun.* 2018, *9*, 488. [CrossRef]
- 49. Wang, X.; Peng, P.; Xuan, W.; Wang, Y.; Zhuang, Y.; Tian, Z.; Cao, X. Narcissistic chiral self-sorting of molecular face-rotating polyhedra. *Org. Biomol. Chem.* **2018**, *16*, 34–37. [CrossRef]
- 50. Wang, Y.; Fang, H.; Zhang, W.; Zhuang, Y.; Tian, Z.; Cao, X. Interconversion of molecular face-rotating polyhedra through turning inside out. *Chem. Commun.* 2017, *53*, 8956–8959. [CrossRef]
- 51. Wang, X.; Wang, Y.; Yang, H.; Fang, H.; Chen, R.; Sun, Y.; Zheng, N.; Tan, K.; Lu, X.; Tian, Z.; et al. Assembled molecular face-rotating polyhedra to transfer chirality from two to three dimensions. *Nat. Commun.* **2016**, *7*, 12469. [CrossRef]
- Zhu, J.-L.; Zhang, D.; Ronson, T.K.; Wang, W.; Xu, L.; Yang, H.-B.; Nitschke, J.R. A Cavity-Tailored Metal-Organic Cage Entraps Gases Selectively in Solution and the Amorphous Solid State. *Angew. Chem. Int. Ed.* 2021, 60, 11789–11792. [CrossRef] [PubMed]
- 53. Séjourné, S.; Labrunie, A.; Dalinot, C.; Benchohra, A.; Carré, V.; Aubriet, F.; Allain, M.; Sallé, M.; Goeb, S. Chiral Self-Sorting in Truxene-Based Metallacages. *Inorganics* **2020**, *8*, 1. [CrossRef]
- Bols, P.S.; Anderson, H.L. Shadow Mask Templates for Site-Selective Metal Exchange in Magnesium Porphyrin Nanorings. *Angew. Chem. Int. Ed.* 2018, 57, 7874–7877. [CrossRef]

- 55. Tehfe, M.-A.; Lalevée, J.; Telitel, S.; Contal, E.; Dumur, F.; Gigmes, D.; Bertin, D.; Nechab, M.; Graff, B.; Morlet-Savary, F.; et al. Polyaromatic Structures as Organo-Photoinitiator Catalysts for Efficient Visible Light Induced Dual Radical/Cationic Photopolymerization and Interpenetrated Polymer Networks Synthesis. *Macromolecules* **2012**, *45*, 4454–4460. [CrossRef]
- Kanibolotsky, A.L.; Berridge, R.; Skabara, P.J.; Perepichka, I.F.; Bradley, D.D.C.; Koeberg, M. Synthesis and Properties of Monodisperse Oligofluorene-Functionalized Truxenes: Highly Fluorescent Star-Shaped Architectures. J. Am. Chem. Soc. 2004, 126, 13695–13702. [CrossRef]
- 57. Guan, J.; Xu, F.; Tian, C.; Pu, L.; Yuan, M.-S.; Wang, J. Tricolor Luminescence Switching by Thermal and Mechanical Stimuli in the Crystal Polymorphs of Pyridyl-substituted Fluorene. *Chem. Asian J.* **2019**, *14*, 216–222. [CrossRef] [PubMed]
- Cohen, Y.; Avram, L.; Frish, L. Diffusion NMR Spectroscopy in Supramolecular and Combinatorial Chemistry: An Old Parameter-New Insights. *Angew. Chem. Int. Ed.* 2005, 44, 520–554. [CrossRef]
- Mirtschin, S.; Slabon-Turski, A.; Scopelliti, R.; Velders, A.H.; Severin, K. A Coordination Cage with an Adaptable Cavity Size. J. Am. Chem. Soc. 2010, 132, 14004–14005. [CrossRef]
- 60. Govindaswamy, P.; Linder, D.; Lacour, J.; Süss-Fink, G.; Therrien, B. Self-assembled hexanuclear arene ruthenium metallo-prisms with unexpected double helical chirality. *Chem. Commun.* **2006**, *45*, 4691–4693. [CrossRef]
- Barry, N.P.E.; Austeri, M.; Lacour, J.; Therrien, B. Highly Efficient NMR Enantiodiscrimination of Chiral Octanuclear Metalla-Boxes in Polar Solvent. Organometallics 2009, 28, 4894–4897. [CrossRef]
- 62. Yuan, M.-S.; Fang, Q.; Liu, Z.-Q.; Guo, J.-P.; Chen, H.-Y.; Yu, W.-T.; Xue, G.; Liu, D.-S. Acceptor or Donor (Diaryl B or N) Substituted Octupolar Truxene: Synthesis, Structure, and Charge-Transfer-Enhanced Fluorescence. *J. Org. Chem.* **2006**, *71*, 7858–7861. [CrossRef] [PubMed]
- 63. Barry, N.P.E.; Furrer, J.; Therrien, B. In and Out of Cavity Interactions by Modulating the Size of Ruthenium Metallarectangles. *Helv. Chim. Acta* **2010**, *93*, 1313–1328. [CrossRef]
- 64. Zhang, H.-N.; Gao, W.-X.; Deng, Y.-X.; Lin, Y.-J.; Jin, G.-X. Stacking-interaction-induced host–guest chemistry and Borromean rings based on a polypyridyl ligand. *Chem. Commun.* **2018**, *54*, 1559–1562. [CrossRef] [PubMed]