

# Entrapment of a dirhodium tetracarboxylate unit inside the aromatic bowl of a calix[4]arene: Unique catalysts for C–H amination†

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Unique calix[4]arene-derived, tetracarboxylate dirhodium(II) inclusion complexes have been prepared and evaluated as catalysts for C–H amination.

Rhodium-catalyzed oxidative amination of saturated C–H bonds has advanced as a valuable method for the construction of stereodefined carbamate centers.<sup>1</sup> The continued evolution of this and related processes, however, necessitates the development of new, robust catalyst systems capable of enhancing reaction yields and influencing product selectivities. Motivated by such pursuits, our group has described the preparation and highlighted the performance of a unique dinuclear Rh(II) catalyst, Rh<sub>2</sub>(esp)<sub>2</sub>. In this complex, a pair of covalently linked carboxylate ligands span *cis*-equatorial sites on the dirhodium center (Fig. 1).<sup>2</sup> The marked stability of Rh<sub>2</sub>(esp)<sub>2</sub> under oxidizing reaction conditions enables C–H amination with sulfamate and carbamate esters to be conducted at low catalyst loadings (0.1–2 mol%) and significantly broadens the scope of this chemistry to include urea, guanidine, and sulfamide substrates.<sup>3,4</sup> Based on these findings, we considered next generation catalyst designs in which three or four carboxylate groups would be affixed to a common frame. From an architectural standpoint, devising a tethered tetracarboxylate ligand for these types of lantern-like dimetallic structures offers an enticing challenge. Herein, we present a strategy aimed at such a goal using a 4-fold symmetric calixarene-based platform. Although the assembled dirhodium complexes differ from the expected form, they are novel structural entities and highly effective catalysts for C–H amination. The modular nature of these complexes has empowered investigations aimed at understanding the influence of the equatorial bridging ligands on catalyst function.

The strict geometrical constraints imposed by the paddlewheel architecture of the Rh<sub>2</sub>(O<sub>2</sub>CR)<sub>4</sub> unit limit the number of practical scaffolds that may be employed to anchor four orthogonally displayed carboxylate ligands. Calix[4]arenes, a readily accessed class of macrocyclic, tetrameric phenols, represent one possible

platform upon which to base such a design.<sup>5–7</sup> The availability of selective methods for the functionalization of calix[4]arenes further enables this plan. Following this rationale, we have exploited the chemistry of calix[4]arenes for the preparation of CLX-H<sub>4</sub>, a unique tetracarboxylate ligand that we hoped would furnish the desired C<sub>4</sub>-symmetric dirhodium complex.

Synthesis of the target ligand is readily accomplished in two steps from a substituted calix[4]arene **1**, and affords CLX-H<sub>4</sub> in high yield (Fig. 2).<sup>8</sup> The four phenolic hydroxyl groups of the lower rim of the calixarene were intentionally left unprotected, as the intramolecular hydrogen bond network established between these moieties sustains the requisite CLX-H<sub>4</sub> “cone” conformation.<sup>5</sup> We anticipated that the strong preorganizational influence of these hydrogen bonds would be critical for achieving selective chelation of the dinuclear Rh core in preference to competing oligomerization processes.

Treatment of Rh<sub>2</sub>(OAc)<sub>4</sub> with CLX-H<sub>4</sub> afforded a single tractable product as a dark green crystalline solid in 67% isolated yield. The <sup>1</sup>H NMR spectrum† of this species, however, was inconsistent with that expected for the product of complete acetate exchange. Two singlets assigned as acetate –CH<sub>3</sub> groups are present in the spectrum (δ = 1.88 and –2.30 ppm), accordant with a complex having the general formula Rh<sub>2</sub>(CLX-H<sub>2</sub>)(OAc)<sub>2</sub>. The extreme upfield shift of one of these signals (–2.30 ppm) gave strong evidence that one acetate ligand was entrapped in the aromatic bowl of the calixarene. Subsequent X-ray crystallographic analysis of Rh<sub>2</sub>(CLX-H<sub>2</sub>)(OAc)<sub>2</sub> confirmed that two carboxylate arms of CLX-H<sub>2</sub> had bridged the dirhodium core in a *trans* orientation (Fig. 3). The two carboxylic acid groups which failed to adopt an equatorial mode of coordination instead occupy both axial sites along the Rh–Rh vector. In all, Rh<sub>2</sub>(CLX-H<sub>2</sub>)(OAc)<sub>2</sub> **2** possesses a most unusual mixed carboxylate ligand set with a rare calixarene-encapsulated acetate unit.<sup>9–11</sup> The

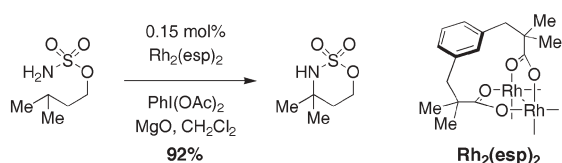


Fig. 1 C–H amination mediated by Rh<sub>2</sub>(esp)<sub>2</sub>.

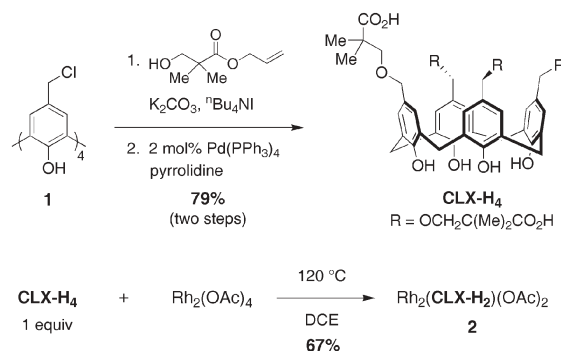
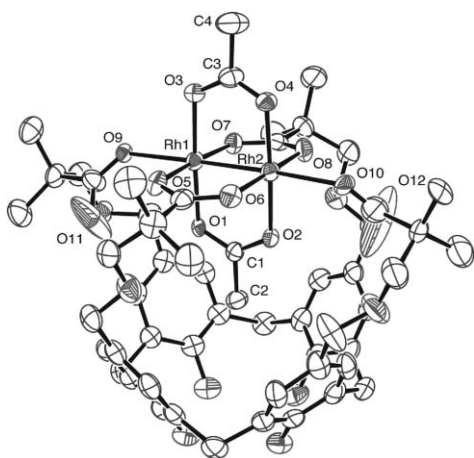


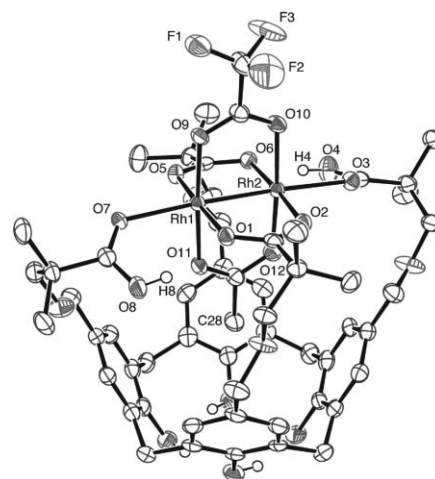
Fig. 2 Synthesis of a novel tetracarboxylate rhodium dimer.

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**Fig. 3** ORTEP representation (50% thermal ellipsoid probability) of  $\text{Rh}_2(\text{CLX-H}_2)(\text{OAc})_2$  **2**. Hydrogen atoms have been omitted for clarity. Selected bond distances (Å) and angles (°): Rh1–Rh2 2.374(3), Rh1–O9 2.311(16), Rh1–O1 2.030(15), Rh2–O4 2.039(16), O7–Rh1–O3 89.5(7), O9–Rh1–Rh2 178.7(4), O2–Rh2–O4 176.5(7).



**Fig. 4** ORTEP representation (50% thermal ellipsoid probability) of  $\text{Rh}_2(\text{CLX-H}_2)(\text{OAc})(\text{O}_2\text{CCF}_3)$  **3**. Selected bond distances (Å) and angles (°): Rh1–Rh2 2.3867(5), Rh1–O7 2.302(3), Rh2–O3 2.301(3), Rh1–O9 2.054(3), Rh1–O11 2.009(3), Rh1–O1 2.035(3), Rh1–O5 2.039(3), O1–O8 2.755(5), O4–O6 2.724(5), O1–H8–O8 164.72, O4–H4–O6 165.68.

measured Rh–Rh bond distance of 2.374 Å is quite similar to those of related dirhodium complexes bearing neutral axial *O*-atom donor ligands.<sup>12</sup>

The ability to substitute one of the four bridging carboxylate ligands selectively in  $\text{Rh}_2(\text{CLX-H}_2)(\text{OAc})_2$  distinguishes this complex from other dirhodium(II) lantern structures. We have found that treating  $\text{Rh}_2(\text{CLX-H}_2)(\text{OAc})_2$  with different carboxylic acids results in the efficient displacement of only the solvent-exposed acetate group (entries 1–6, Table 1). These new complexes represent the first series of dinuclear Rh(II) adducts to bear three disparate bridging carboxylate types. Single crystal X-ray analysis of one of these,  $\text{Rh}_2(\text{CLX-H}_2)(\text{OAc})(\text{O}_2\text{CCF}_3)$  **3** (entry 1), shows the trifluoroacetate moiety positioned opposite the encapsulated acetate (Fig. 4). Also apparent in this structure are intramolecular H-bonds between the protons of the axial carboxylic acid ligands and the bridging carboxylate groups (e.g., O8–H8–O1).

Presumably, these H-bond contacts provide additional stabilization to the complex.<sup>13</sup> This image also captures what is possibly a snap-shot of the mechanism by which carboxylic acids exchange from axial to bridging equatorial coordination modes, and likely explains why all four carboxylate arms of the calixarene do not adopt a bridging coordination mode.<sup>14</sup>

Importantly, the lability of the trifluoroacetate ligand in **3** facilitates selective metathesis reactions with hydroxypyridine and carboxamide ligands (entries 7 and 8, Table 1), thus giving rise to truly unique carboxylate–amidate hybrid structures. The ability to vary a single carboxylate with other bridging groups should help forward efforts to elucidate pathways for catalyst decomposition *vis-à-vis* ligand dissociation under the oxidizing conditions of our C–H amination reaction.

A particularly striking and unanticipated feature of these dirhodium complexes is the unprecedented *trans* relationship between the two bridging carboxylate groups of CLX-H<sub>2</sub>. To the best of our knowledge, all polycarboxylate ligands used to form such lantern structures are linked to the metal centers in a *cis*-orientation, as in the case of  $\text{Rh}_2(\text{esp})_2$  (Fig. 1).<sup>15</sup> We suspected that the mechanism for assembly of these unusual CLX-H<sub>2</sub> complexes may initiate through non-covalent association between a methyl group of the  $\text{Rh}_2(\text{OAc})_4$  starting material and the calixarene pocket. As observed crystallographically in both **2** and **3**, distances of 3.6–4.0 Å from the  $\alpha$ -carbon to the centroids of the arene rings are indicative of strong C–H/ $\pi$  interactions.<sup>16</sup> To investigate the self-assembly process, metathesis reactions were conducted using CLX-H<sub>4</sub> and a series of  $\text{Rh}_2(\text{O}_2\text{CR})_4$  adducts. Due to the small volume of the calixarene cavity, CLX-H<sub>4</sub> fails to entrap larger carboxylate groups such as those in  $\text{Rh}_2(\text{O}_2\text{CC}_2\text{H}_5)_4$  and  $\text{Rh}_2(\text{O}_2\text{CCF}_3)_4$ . When using these starting materials, only intractable polymeric materials are formed. Conversely, the complex derived from  $\text{Rh}_2(\text{O}_2\text{CH})_4$  can be generated, but in very poor yield (18%). Such data intimate that cooperative non-covalent interactions between the aromatic bowl of CLX-H<sub>4</sub> and guest ligands are critical for the efficient assembly of these supramolecular systems.

**Table 1** Selective ligand metathesis reactions<sup>a</sup>

<p><b>2:</b> R = CH<sub>3</sub>  <b>3:</b> R = CF<sub>3</sub></p> <p><math>\text{Rh}_2(\text{CLX-H}_2)(\text{OAc})(\text{XC(O)R}')</math></p>			
Entry	R'C(O)XH	Starting Complex	Yield [%]
1	CF <sub>3</sub> CO <sub>2</sub> H	<b>2</b>	85
2	C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> H	<b>2</b>	84
3	Ph <sub>3</sub> CCO <sub>2</sub> H	<b>2</b>	80
4	<i>o</i> -PhC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> H	<b>2</b>	81
5	<i>p</i> -VinylC <sub>6</sub> H <sub>4</sub> CO <sub>2</sub> H	<b>2</b>	91
6	1-AdCO <sub>2</sub> H <sup>b</sup>	<b>2</b>	79
7	2-Hydroxypyridine	<b>3</b>	67
8	C <sub>6</sub> H <sub>5</sub> C(O)NH <sub>2</sub>	<b>3</b>	47

<sup>a</sup> A representative illustration of the dirhodium complex viewed down the Rh–Rh axis. Typical reaction conditions employ 5 equiv of R'C(O)XH, see supporting information for more details.

<sup>b</sup> 1-AdCO<sub>2</sub>H = 1-adamantylcarboxylic acid.

**Table 2** Comparative data for C–H amination mediated by CLX-based Rh<sub>2</sub> complexes<sup>a</sup>

<div style="display: flex; justify-content: space-around; margin-top: 10px;"> <div> <p><b>A:</b> R<sup>1</sup> = R<sup>2</sup> = Me</p> <p><b>B:</b> R<sup>1</sup> = Ph, R<sup>2</sup> = H</p> <p><b>C:</b> R<sup>1</sup> = Me, R<sup>2</sup> = H</p> </div> </div>				
Entry	Catalyst	Substrate	Conversion [%]	Yield [%]
1	Rh(C LX-H <sub>2</sub> )(OAc) <sub>2</sub>	<b>A</b>	100	93
2	Rh(C LX-H <sub>2</sub> )(OAc)(O <sub>2</sub> CCF <sub>3</sub> )	<b>A</b>	<10	—
3	Rh(C LX-H <sub>2</sub> )(OAc) <sub>2</sub>	<b>B</b>	90	81
4	Rh(C LX-H <sub>2</sub> )(OAc)(O <sub>2</sub> CCF <sub>3</sub> )	<b>B</b>	<10	—
5	Rh(C LX-H <sub>2</sub> )(OAc)(O <sub>2</sub> CCPh <sub>3</sub> )	<b>B</b>	95	88
6	Rh(C LX-H <sub>2</sub> )(OAc) <sub>2</sub>	<b>C</b>	65	58
7	Rh(C LX-H <sub>2</sub> )(OAc)(O <sub>2</sub> CCPh <sub>3</sub> )	<b>C</b>	80	69
8	Rh(C LX-H <sub>2</sub> )(OAc)(O <sub>2</sub> CAd) <sup>b</sup>	<b>C</b>	65	—
9	Rh <sub>2</sub> (O <sub>2</sub> CC <sup>t</sup> H <sub>15</sub> ) <sub>4</sub>	<b>C</b>	20	—
10	Rh <sub>2</sub> (O <sub>2</sub> CCPh <sub>3</sub> ) <sub>4</sub>	<b>C</b>	10	—
11	Rh <sub>2</sub> (esp) <sub>2</sub> <sup>c</sup>	<b>C</b>	100	90

<sup>a</sup> Reactions performed with 1.1 equiv of PhI(OAc)<sub>2</sub> and 2.3 equiv of MgO at 0.15 M [substrate] in CH<sub>2</sub>Cl<sub>2</sub>. Conversion percentages are estimated based on integration of the <sup>1</sup>H NMR of the unpurified reaction mixture. <sup>b</sup> Ad = 1-adamantyl. <sup>c</sup> Rh<sub>2</sub>(esp)<sub>2</sub> = Rh<sub>2</sub>(α,α',α'',α'-tetramethyl-1,3-benzenedipropionate)<sub>2</sub>, see ref. 2.

The catalytic performance of the calixarene-based complexes for the oxidative amination of C–H bonds is higher than almost all other dinuclear Rh systems tested (Table 2). Of these, only Rh<sub>2</sub>(esp)<sub>2</sub> has proven more effective (entry 11). Interestingly, catalyst turnover expresses a noted dependence on the steric and electronic structure of the solvent-exposed mono-carboxylate ligand. As an example, Rh<sub>2</sub>(CLX-H<sub>2</sub>)(OAc)(O<sub>2</sub>CCF<sub>3</sub>) **3**, with its highly labile trifluoroacetate group, is entirely ineffective when tested against two sulfamate esters (entries 2 and 4, Table 2). This finding suggests that partial or complete dissociation of a single bridging ligand may trigger catalyst decomposition. Conversely, Rh<sub>2</sub>(CLX-H<sub>2</sub>)(OAc)(O<sub>2</sub>CCPh<sub>3</sub>) exhibits greater stability and higher turnover numbers when compared to the parent diacetate complex (entries 5 and 7). Studies to determine the precise mechanistic reasons for these phenomena are currently in progress.

A unique family of dirhodium complexes supported by the tetracarboxylate ligand CLX-H<sub>4</sub> is described. Favorable non-covalent interactions between the methyl group of an acetate ligand and the aromatic walls of the calixarene frame make possible the efficient assembly of these unprecedented lantern structures. A second acetate bridge, which sits opposite the calixarene, is readily exchanged with different carboxylate groups. These mixed-carboxylate systems have been tested as catalysts for C–H amination and display estimable performance when compared to other known Rh dimers. Accordingly, access to disparate dirhodium complexes based on the multidentate CLX-H<sub>4</sub> ligand will aid investigations to reveal the complex process(es) that lead to catalyst inactivation and decomposition in these C–H oxidation reactions. We anticipate that such insights will give way to subsequent methodological advances for both intra- and inter-molecular C–H functionalization chemistry.

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- A) 2-EtOAc: C<sub>60</sub>H<sub>76</sub>O<sub>22</sub>Rh<sub>2</sub>: M<sub>r</sub> = 1355.03, orthorhombic, space group P<sub>bcn</sub>, a = 20.989(3), b = 19.577(3), c = 29.775(4) Å, V = 12235(3) Å<sup>3</sup>, Z = 8, T = 170 K, 66 886 reflections measured, 12 453 unique (R<sub>int</sub> = 0.0490), μ = 0.62 cm<sup>-1</sup>, R<sub>1</sub> = 0.0903, wR<sub>2</sub> = 0.2045 for F<sub>0</sub> > 4σ(F<sub>0</sub>). The hydroxyl groups of the axially disposed carboxylic acid ligands display significant positional disorder, suggesting two H-bond interactions with proximal carboxylate ligands. B) 3-Et<sub>2</sub>O: C<sub>60</sub>H<sub>75</sub>F<sub>3</sub>O<sub>21</sub>Rh<sub>2</sub>: M<sub>r</sub> = 1395.02, triclinic, space group P $\bar{1}$ , a = 11.144(1), b = 15.847(2), c = 17.717(2) Å, α = 86.286(2), β = 88.553(2), γ = 86.249(2)°, V = 3115.0(5) Å<sup>3</sup>, Z = 2, T = 170 K, 20 750 reflections measured, 12 496 unique (R<sub>int</sub> = 0.0397), μ = 0.61 cm<sup>-1</sup>, R<sub>1</sub> = 0.0526, wR<sub>2</sub> = 0.1370 for F<sub>0</sub> > 4σ(F<sub>0</sub>). CCDC 606038 and CCDC 606037. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b611280c.
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