Synthesis and structural characterization of 20-membered macrocyclic rings bearing trans-chelating bis(N-heterocyclic carbene) ligands and the catalytic activity of their palladium(II) complexes

Journal:	*Dalton Transactions*
Manuscript ID	DT-ART-05-2019-002147.R3
Article Type:	Paper
Date Submitted by the Author:	18-Jul-2019
Complete List of Authors:	Thapa, Rajesh; University of Arkansas Fayetteville, Chemistry and Biochemistry Kilyanek, Stefan; University of Arkansas Fayetteville, Chemistry and Biochemistry

SCHOLARONE™
Manuscripts

ARTICLE

Synthesis and structural characterization of 20-membered macrocyclic rings bearing *trans*-chelating bis(N-heterocyclic carbene) ligands and the catalytic activity of their palladium(II) complexes

Rajesh Thapa and Stefan M. Kilyanek*[a]

Macrocycles consisting of a 20-membered ring containing two imidazolium salt functionalities and of the formula [PhCH$_2$N(CH$_2$CH$_2$CH$_2$)Im(CH$_2$CH$_2$CH$_2$)$_2$][Br]$_2$ (Im = imidazole = **3a**, benzimidazole = **3b**) were synthesized in 70-75% yields. These salts serve as precursors to macrocycles containing two N-heterocyclic carbene (NHC) moieties. Reaction of the macrocyclic salts **3a** and **3b** with silver oxide afforded macrocyclic-bis(NHC)silver(I) complexes **4a** and **4b**. Single-crystal X-ray diffraction studies of macrocyclic-bis(NHC)silver(I) complex **4a** revealed a tetranuclear silver core with a short Ag-Ag distance (2.9328 Å). Complexes **4a** and **4b** serve as carbene transfer reagents to Pd. The treatment of macrocyclic-bis(NHC)silver(I) complexes **4a** and **4b** with one equivalent of PdCl$_2$(MeCN)$_2$ in methylene chloride afforded square-planar *trans*-macrocyclic-bis(NHC)Pd(II)X$_2$ complexes **5a** and **5b**. Preliminary screening of these palladium complexes showed they are competent precatalysts for Heck and Suzuki coupling reactions.

Introduction

After the isolation of the first stable, free N-heterocyclic carbenes (NHCs) by Arduengo,[1] NHCs have been used widely in homogenous catalysis and coordination chemistry. Due to their strong σ-donating properties, NHC ligands bind strongly to a variety of metals and stabilize a wide range of metal oxidation states.[2,3,4] NHC complexes owe their high thermal stabilities to their strong metal-carbon bonds, and NHC ligands are unique due to their lack of π-accepting properties.[5,6] For these reasons, NHCs have found a wide range of applications where phosphine ligands are not desirable.[7-10] The NHC moiety has been shown to coordinate to most transition metals and has been used as a supporting ligand for a wide variety of catalysts with excellent performance in many important reactions.[6,11-13] NHCs have been shown to coordinate with Pd, generating competent precatalysts for C-C bond-forming reactions.[14-22]

Although there has been an abundance of work on the synthesis and reactivity of NHC-metal complexes, there is still significant interest in the development of new macrocyclic NHC ligands.[2,3,5,12,14,20,23,24] There is an abundance of research on *cis*-bidentate-chelating NHC ligands with Pd; fewer ligands have been reported that coordinate in a *trans* fashion, and still fewer within a closed (macrocyclic) scaffold.[18,25-29] The first *trans*-chelated bis(NHC) complexes of Pd and Ni possessing binaphthyl backbones were reported by RajanBabu.[30] This

ligand formed a mixture of *cis*- and *trans*-chelated Pd NHC complexes. The *cis/trans* mixture is common and cannot be separated in most cases.[27,31] Pd complexes with bidentate *trans*-chelating NHCs have been shown to be active catalysts for C-C coupling reactions.[32,18]

Douthwaite et al. discovered flexible tridentate bis-NHC amino ligands where the NHC moieties are connected by a flexible five-atom linker consisting of four methylene groups and an amino functionality (CH$_2$CH$_2$NRCH$_2$CH$_2$). They showed that these ligands bind to the Pd center as a tridentate pincer with coordination of the central amine.[32,33] Hazari et al. reported a family of bidentate *trans*-chelating NHC ligands with flexible propyl linkers incorporating a tertiary amine. They have shown that these ligands easily bind to Pd in a bidentate *trans*-spanning fashion with no coordination to the central amine, forming a 12-membered palladacycle (Chart 1, i).[18] These Pd complexes are active towards Heck and Suzuki reactions.[18,32,33]

A macrocyclic complex with a 15-membered ring and a bidentate cyclophane geometry containing a butane linker was reported (Chart 1, ii) by Hahn.[34] A plethora of small 15-membered macrocyclic complexes[31,34,35] or larger 28-38 membered macrocyclic ligands[36,37] with tridentate coordination systems have been reported, but only a handful of "intermediate" sized macrocyclic ligands are in the literature. Chaplin and co-workers have synthesized a series of 19-23-membered CNC macrocyclic pincer ligands consisting of bis(imidazolium)-lutidine salts with octa-, deca- and dodecane spacers (Chart 1, iii). These CNC macrocyclic pincer ligands are converted to Ag carbene complexes that serve as transmetalating agents to produce cationic Pd(II) chloride

[a.] *Department of Chemistry and Biochemistry, 1 University of Arkansas, Fayetteville, AR 72701*

complexes.[38] Pd complexes comprised of 16-member macrocycles containing two or more NHC's have been synthesized by Pöthig and Kühn (Chart 1, iv)[39] in addition to macrocycles containing other transition metals.[40] These macrocyclic systems differ from the others discussed here because they are rigid and do not contain any available coordination sites at the metal. Other groups have synthesized macrocycles containing two or more NHC moieties of similar size.[41] Additionally, Kühn and co-workers have synthesized larger more flexible systems that are analogous to their macrocyclic systems but do not consist of a closed macrocycle.[42] These flexible ligand systems can coordinate a variety of metals and some can coordinate several metal centers.[43]
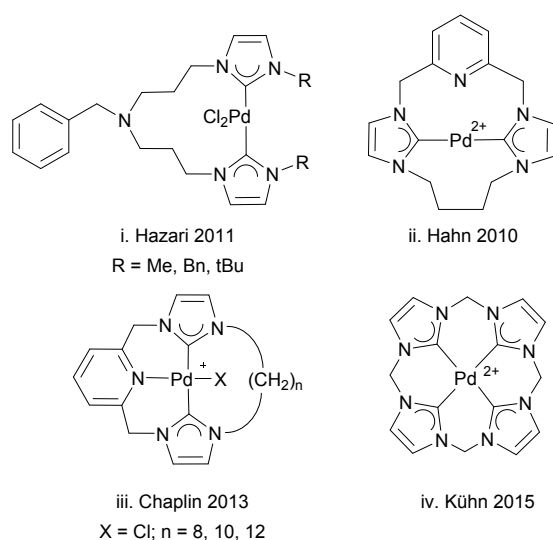

**Chart 1.** Previously reported polydentate and macrocyclic (NHC)Pd(II) complexes

As mentioned above, some of these polydentate ligands have been observed to adopt a variety of coordination modes by displacement of inner sphere halides.[38,32,33] The ligands in this study were chosen to have a larger ring structure than those of Hahn and co-workers. These larger ring structures are expectedly fluxional. Additionally, the larger ring structures used in this study differ from Chaplin and Hahn's previous work because these macrocycles contain four possible coordination sites, enabling these macrocycles to adopt a number of coordination modes and stereochemistries.

In this study, we examined the coordination chemistry and reactivity of intermediate-sized 20-membered macrocyclic rings containing two tertiary amines and two NHC moieties derived from imidazole and benzimidazole. We synthesized and characterized the silver(I) complexes of these macrocyclic ligands for use as carbene transfer / transmetalating agents. We surveyed the coordination chemistry of these ligands with Pd as a first step toward understanding whether these intermediate-sized rings would adopt a mixture of stereoisomers (*cis / trans* NHCs) or form mixtures of coordination modes to the metal (κ^2, κ^3 etc.). In particular, the displacement of inner-sphere halides to form cationic metal species is of interest for Pd and other transition metals. This work lays the foundation for studies of the coordination chemistry of these intermediate-sized

macrocycles with a broad array of metals. We found that these macrocycles adopt *trans*-NHC configurations when coordinated to Pd. The flexible *trans* amino ligands connected to the NHCs by propyl chains were not found to displace inner sphere halides of the Pd complexes in the solid state. We have characterized these Pd complexes and screened them for activity as precatalysts for Suzuki-Miyauri and Heck cross-coupling reactions.

Results and Discussion

Scheme 1 summarizes the synthesis of the bis-imidazole amine and bis-benzimidazole amine compounds (**2a-2b**) that comprise half of the target 20-member macrocycles as well as macrocycles **3a** and **3b**. Bis(ester) (**A**) was synthesized from commercially available benzylamine and ethyl acrylate utilizing a Michael addition.[44] Reduction of **A** with LiAlH$_4$ produced bis(alcohol) (**B**),[18] which was converted into the bis-bromide starting material (**1**) by refluxing with concentrated HBr for 24 hours.[45] N-Benzylbis(3-bromopropyl)-imidazole (**2a**) and N-benzylbis(3-bromopropyl)benz-imidazole (**2b**) were obtained by the reaction of N-benzylbis(3-bromopropyl)amine **1**, sodium hydride and imidazole or benzimidazole, respectively, in THF (Scheme 1). Both compounds **2a** and **2b** are colorless viscous liquids.
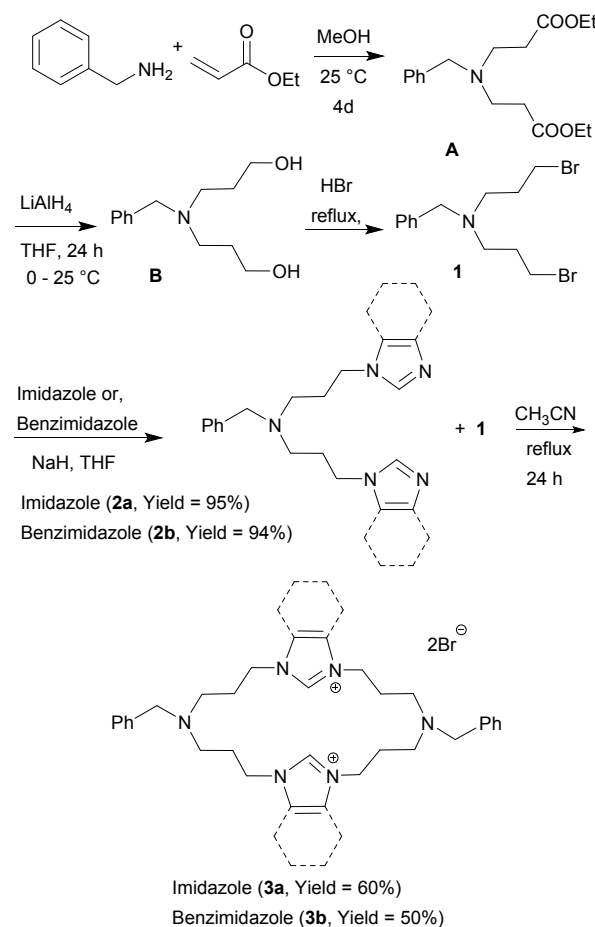

Imidazole (**3a**, Yield = 60%)
Benzimidazole (**3b**, Yield = 50%)
Scheme 1. Synthesis of macrocyclic ligand **3a** and **3b**

ARTICLE

The cyclization reaction between **1** and N-benzylbis(3-bromopropyl)-imidazole **2a** or N-benzylbis(3-bromopropyl)benzimidazole **2b** yields the corresponding cyclophane-like 20-membered macrocyclic bisimidazolium bromide salts **3a** and **3b** (Scheme 1). The cyclization reactions were performed at low concentrations (~100 mM) to prevent possible oligomerization side reactions.[18]

Proligand **3a** is a hygroscopic white solid, which is soluble in polar solvents such as dichloromethane, acetonitrile, and THF and insoluble in nonpolar solvents such as toluene, hexanes, and petroleum ether. Unlike **3a**, the proligand **3b** is stable in air and is soluble in chloroform, but is insoluble in methylene chloride, acetonitrile, and dimethyl sulfoxide. The overall yield of **3a**-**3b** is 50 to 60%.

A crystal suitable for X-ray crystallography of **3a** was obtained by slow diffusion of chloroform into a solution of **3a** in dichloromethane (Figure 1). The X-ray structure confirms macrocycle formation. ^{1}H NMR spectroscopy of **3a** in CD_2Cl_2 shows three resonances at δ 4.05 (triplet), δ 2.49 (triplet) and δ 1.97 (quintet) ppm. These resonances correspond to the three methylene groups of the four propyl chains ($NCH_2CH_2CH_2N$) present in the macrocyclic proligand **3a** Similarly, three resonances were observed for the methylene protons of the propyl chains of **3b** in $CDCl_3$ at δ 4.64 (triplet), δ 2.83 (triplet) and δ 2.65 (quintet) ppm. These data show that the solution conformations of **3a** and **3b** are either highly fluxional or are consistent with the symmetric structures observed in the solid state.

The ^{1}H NMR resonances of the imidazolium 2-position protons (NCHN) for **3a** and **3b** appear as singlets at δ 10.77 ppm and δ 11.33 ppm, respectively. ^{13}C NMR shows the C-H resonances of the imidazolium 2-position at δ 139 ppm (**3a** in CD_2Cl_2) and δ 144 ppm (**3b** in $CDCl_3$). These chemical shifts are consistent with similar systems in the literature.[46]
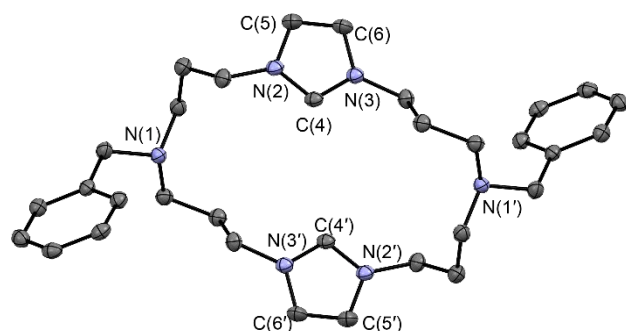
Figure 1. Thermal ellipsoid plot of the diimidazolium salt, $C_{32}H_{44}Br_2N_6\cdot2(CHCl_3)$, **3a** (50% ellipsoids). Hydrogen atoms, bromide anions and solvent molecules have been omitted for clarity. The two sides of the macrocycle were found to be equivalent by symmetry.

Attempts to deprotonate proligand **3a** to form a macrocyclic bis-NHC compound were not successful on large scales. An NMR tube reaction between proligand **3a** and excess sodium hydride in DMSO-d_6 showed the formation of free bis-NHC **3c** in situ under nitrogen atmosphere at room temperature. The in situ generation of the free bis-NHC **3c** was confirmed by a

characteristic downfield ^{13}C NMR peak at δ 208 ppm corresponding to a free carbene. Additionally, the ^{1}H NMR signal for the imidazolium 2-position previously observed at δ 9.19 ppm is no longer present, implying formation of the free carbene **3c**. The free bis-NHC ^{13}C NMR carbene chemical shift observed is comparable to the isolable NHC (δ 211.43 ppm in C_6D_6) reported by Arduego et al.[1] and other NHCs.[46]

Attempts to isolate the free carbene furnished an intractable viscous dark red oil consistent with the literature.[32] This oil can be generated through deprotonation of the imidazolium salt **3a** using bases such as t-BuOK and/or NaH. However, subsequent work-up results in decomposition and the formation of multiple products. As reported previously,[12] this product mixture was likely formed by deprotonation of the benzylic positions of the macrocycle and deprotonation of the methylene groups adjacent to the imidazole rings.

Direct reaction of free carbenes generated in situ by treatment of a mixture of imidazolium salt and strong base with $PdCl_2(MeCN)_2$ has been shown to yield metalated product.[47] Direct reaction of in situ generated **3c** with $PdCl_2(MeCN)_2$ yielded a mixture of products. Several bases were screened for direct deprotonatation and metalation of the ligand including n-BuLi, NaH, t-BuOK. All these reactions yielded a mixture of products. Reaction of **3b** with t-BuOK in THF with $PdCl_2(MeCN)_2$ also yields a complex product mixture. Additionally, direct metalation of **3a** and **3b** with $PdCl_2(MeCN)_2$ did not occur after refluxing 16 hours in methylene chloride.
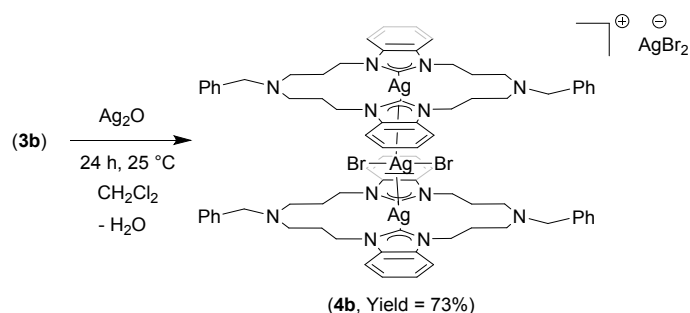
Ag complexes

Several groups have used transmetalation from Ag complexes as a strategy to efficiently synthesize other metal NHC complexes.[38,48-57] Bis(NHC)silver(I)bromide complexes **4a** and **4b** were prepared as ligand transfer agents (Schemes 2 and 3) by the reaction of imidazolium salts **3a** and **3b** with excess silver oxide in methylene chloride. Upon deprotonation of **3a** and **3b,** the target 20-member macrocyclic bis-NHC-bis-amino ligands are formed and coordinate to Ag(I).
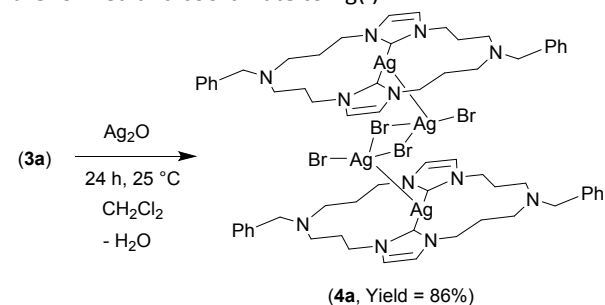
Scheme 2. Synthesis of bis(NHC)Ag(I)bromide complexes **4a**

Analytically pure, light-sensitive Ag complexes **4a** and **4b** were obtained in high yield as white crystalline solids. After the reaction of silver oxide with solutions of **3a** and **3b** for 24 hours, the imidazolium 2-position ^{1}H NMR resonances were no longer present. Additionally, the characteristic ^{13}C NMR signals of the C-H 2-position of imidazolium compounds **3a** and **3b** were shifted downfield from 139 and 144 ppm to 180 and 181 ppm for the Ag complexes **4a** and **4b,** respectively. This downfield shift is characteristic of Ag-NHC complexes.[18,46]

Scheme 3. Synthesis of bis(NHC)Ag(I)bromide complexes **4a** and **4b**

The ^{1}H NMR spectra of **4a** and **4b** show four methylene resonances consistent with a benzylic methylene group and three methylene resonances from the propyl chains of the macrocycle. These data show that both sides of the macrocycle and all four propyl chain linkers are equivalent, implying that the Ag carbene macrocycle is fluxional in solution. The absence of Ag-^{13}C coupling also suggests that **4a** and **4b** linkers are fluxional and that the Ag-carbene bond is labile on the NMR timescale.[57,58 60]
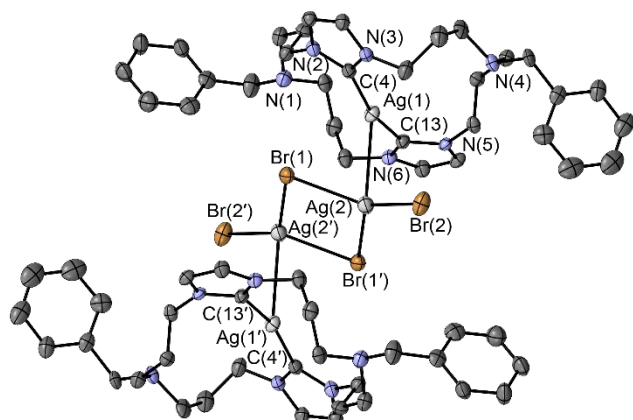

Figure 2. Thermal ellipsoid plot of silver complex **4a** with thermal ellipsoids at 50% probability. Hydrogen atoms have been removed for clarity. Selected bond distances (Å) and bond angles (°): Ag(1)-Ag(2) = 2.9327(18), Ag(2)-Br(1) = 2.6802(19), Ag(2)-Br(2) = 2.5370(19); C(4)-Ag(1)-Ag(2) = 123.0(3), Br(2)-Ag(2)-Br(1) = 126.42(6), Br(2)-Ag(2)-Ag(1) = 91.60(5)

Ag-NHC complexes have been shown to exhibit a variety of binding modes in the solid state.[18,25,61] In order to determine the nucleariety of the complexes, the structures were investigated by single-crystal X-ray diffraction analysis.

A colorless crystal suitable for X-ray crystallography of **4a** was obtained by slow diffusion of chloroform into a saturated dichloromethane solution of **4a**. As shown in Figure 2, **4a** exists as a dimer consisting of two crystallographically equivalent macrocyclic ligands, each chelating a single silver atom through the NHC moieties of the macrocycle. These Ag-macrocycle complexes are bridged by a dianionic core which consists of a $[Ag_2Br_4]^{2-}$ unit. This bridging $[Ag_2Br_4]^{2-}$ unit is well known in the literature.[18,25,50,59,61,62-64] The C(4)-Ag(1)-C(13) angle (NHC-Ag NHC angle) was found to be 163.4°, showing the coordinated Ag atom protruding from the center of the macrocycle. Notably, the distance between the chelated Ag atoms within the

macrocycles and the Ag atoms of the $[Ag_2Br_4]^{2-}$ core is only is 2.9328(18) Å, which is shorter than bond lengths reported for similar Ag complexes and is indicative of Ag-Ag bonding.[18,25,58] This short Ag(1)-Ag(2) bond distance may explain the acute angle observed for (C(4)-Ag(1)-C(13)), as if the bonding to the $Ag_2Br_4^{2-}$ core is pulling the chelated Ag away from the center of the macrocycle.
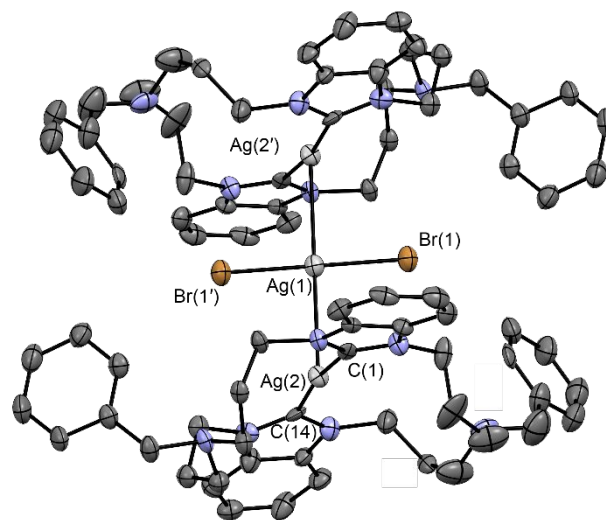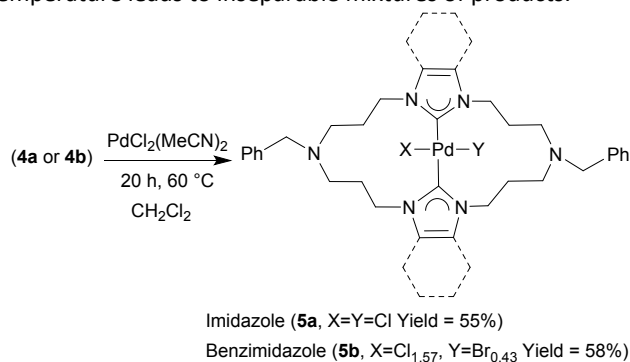

Figure 3. Thermal ellipsoid plot of silver complex **4b** with thermal ellipsoids at 50% probability. Hydrogen atoms, AgBr₂⁻, and solvent molecules have been removed for clarity. Selected bond distances (Å) and bond angles (°): Ag(1)-Br(1) = 2.450(4), Ag(1)-Ag(2) = 3.005(3); Ag(2')-Ag(1)-Ag(2) = 180.0, Br(1)-Ag(1)-Ag(2') = 97.73(8), Br(1')-Ag(1)-Br(1) = 180.00(6).

A crystal suitable for single-crystal X-ray diffraction of **4b** was obtained by slow evaporation of a saturated dichloromethane solution of macrocyclic-bis(NHC)silver(I) bromide **4b**. In the solid state structure of **4b** (Figure 3), two structurally equivalent cationic macrocyclic-bis(NHC)silver(I) complexes are linked through an anionic AgBr₂⁻ core. A second AgBr₂⁻ unit is found in the unit cell; however, no close contacts are observed to the second anion. The AgBr₂⁻ unit linking the two macrocyclic Ag complexes appears to be perfectly linear. The Br(1)-Ag(1)-Ag(2) angle of 97.94° shows that the bridging Ag(1) atom possess a slightly distorted square planar geometry. Unlike **4a,** the Ag(1)-Ag(2) bond distance of 3.004(3) Å is consistent with literature reports of Ag-Ag bond distances in similar compounds.[61] Additionally, the C(14)-Ag(2)-C(1) angle was found to be 170.30°, which is larger than the analogous angle in **4a**. This AgBr₂⁻ anionic core bridging between Ag-NHC complexes is commonly seen as part of larger coordination-polymer crystal systems in the literature.[61] However, it does not appear to be as common for dimeric structures.[65]

Palladium complexes

Metal acetates have been used to synthesize NHC complexes without isolation of the free carbene. Hermann et al. reported the first structurally characterized *trans*-bis(NHC)Pd(II)Cl₂ complex that was prepared by direct deprotonation of imidazolium salts with palladium acetate.[66,34,64] In our hands, the direct deprotonation of imidazolium salts **3a** and **3b** with

palladium(II) acetate and platinum(II) acetylacetonate at high temperature leads to inseparable mixtures of products.

Imidazole (**5a**, X=Y=Cl Yield = 55%)
Benzimidazole (**5b**, X=Cl$_{1.57}$, Y=Br$_{0.43}$ Yield = 58%)

Scheme 4. Synthesis of bis(NHC)Pd(II)Cl$_2$ complexes **5a** and **5b**

Pd complexes **5a** and **5b** were prepared by the reaction of bis(NHC)silver(I) bromide complexes **4a** and **4b** with PdCl$_2$(MeCN)$_2$ (Scheme 4). After 20 hours at 60 °C, the reaction forms silver bromide as a pale yellow precipitate. Bis(NHC)Pd(II)Cl$_2$ complexes **5a** and **5b** were obtained as white solids after removal of silver bromide by filtration and evaporation of solvent (Scheme 4).
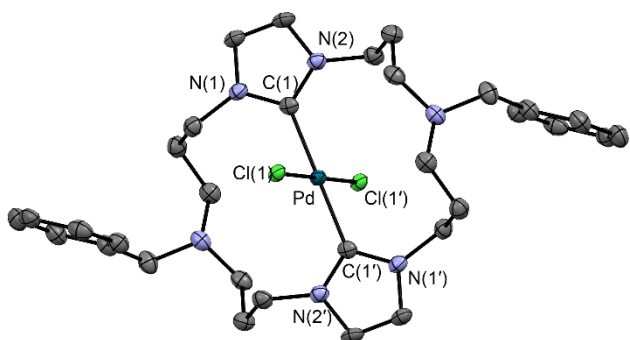
Figure 4. Thermal ellipsoid plot of **5a** with thermal ellipsoids at 50% probability. Hydrogen atoms have been removed for clarity. Selected bond distances (Å) and bond angles (°): Pd(1)-Cl(1)= 2.3387(9), Pd(1)-C(1) = 2.031(3), C(1)-N(1) = 1.352(4); Cl(1)-Pd(1)-Cl(1') = 180.00(2), C(1)-Pd(1)-Cl(1) = 90.05(9), C(1)-Pd(1)-C(1') = 180.0

A crystal of **5a** suitable for X-ray crystallography was obtained by slow diffusion of pentane into a saturated dichloromethane solution of the Pd compound. The X-ray structure (Figure 4) confirms that the NHC moieties of the macrocycle coordinate in a *trans* fashion. **5a** was found to possess a C$_2$-symmetric structure. Additionally, no coordination is observed from the pendant amines in the macrocycle to the Pd center. The [C(1)-Pd-C(1')] angle was found to be 180.00°, and the Pd center has a nearly ideal square-planar geometry, in contrast to Hazari's similar complexes.[18] Additionally, the observed bite angle of the ligand is larger than that of many Pd complexes with *trans*-spanning phosphine ligands.[67] The two pendant amine groups within the macrocycle are positioned directly above and below the Pd-NHC coordination plane, as if approaching the Pd along the idealized z-axis of the square-planar complex. The amine N-Pd distance was found to be 3.746(2) Å.

X-ray diffraction of **5b** (Figure 5) shows a *trans* configuration for the NHC moieties of the macrocyclic ligand with no coordination

of the pendant amines to Pd. Additionally, X-ray diffraction shows that **5b** exists as a mixed halide species with a stoichiometry of C$_{40}$H$_{46}$N$_6$PdCl$_{1.57}$Br$_{0.43}$. ^{1}H NMR spectra of typical preparations of **5b** show only one set of peaks for **5b**. HR-FT-ICR-MS shows the monochloride mono cation [C$_{40}$H$_{46}$ClN$_6$Pd]$^+$: m/z 751.2508 (calcd) and 751.2528 (found). Mixtures of halomers have been previously observed as a result of various synthetic methods to generate late metal carbene species including transmetalation from silver salts.[68]

The structure of **5b** is comparable to the solid-state structure of **5a** (Figure 4). Both structures show nearly ideal square-planar coordination of Pd. The stereochemistry of the Pd center is likely related to the ring size of the macrocycle, specifically, the number of methylene linkers in the chains between the two NHC moieties. The *cis* isomer appears to be favored in shorter linkers.[18,64] A minimum of six methylenes as linker is suggested to favor *trans* coordination by DFT studies,[18] consistent with our observations.

The macrocyclic ligands in **5a** and **5b** appear to completely envelop the Pd center. The torsion angles between the square planes of the Pd(II) center and the planes of the NHC rings are 115.5° and 108.9°, respectively. Effectively, the Pd-Cl bonds protrude from the plane of the macrocyclic structure surrounding the Pd center. The distances between the Pd and amine N atoms in **5a** and **5b** are 3.746 Å and 3.825 Å, which are well beyond the sum of the van der Waals radii of Pd and N (3,18 Å).[73,69] It is reasonable to assume that these large distances allow ample space for reactions to occur at Pd (*vide infra*).
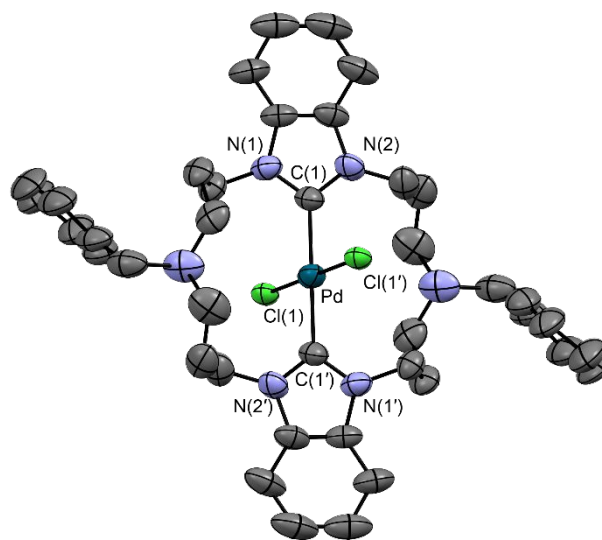
Figure 5. Thermal ellipsoid plot of carbene complex **5b** with thermal ellipsoids at 50% probability. Hydrogen atoms, a disordered phenyl group and a partially occupied Br have been omitted for clarity. Selected bond distances (Å) and bond angles (°): Pd-Cl(1)= 2.241(16), Pd-C(1) = 2.027(12), C(1)-N(1) = 1.343(15); Cl(1)-Pd(1)-Cl(1') = 180.0, C(1)-Pd(1)-Cl(1) = 89.3(6).

Pd-catalyzed coupling reactions

The Suzuki reaction, the coupling of an aryl halide with phenylboronic acid, is one of the most widely known cross-coupling reactions.[70] The macrocyclic-*trans*-bis(NHC)PdCl$_2$

complexes **5a** and **5b** were screened for activity as precatalysts for Suzuki and Heck cross-coupling reactions. The reaction conditions for the Suzuki and Heck reactions are described in the experimental procedures and were modified from the literature.[18,71] The products were detected by gas chromatography-mass spectroscopy (GC/MS) and the percentage yield was calculated by comparing the proton resonance of the product with the known proton resonance of an internal standard (1,3,5-trimethoxybenzene).

The Suzuki coupling of aryl halides with phenylboronic acid (Scheme 5) was performed using 1 mol % of the Pd precatalyst (Table 1).

X = Cl, Br, I

R = H, CH₃, -COCH₃, -OCH₃, -NO₂
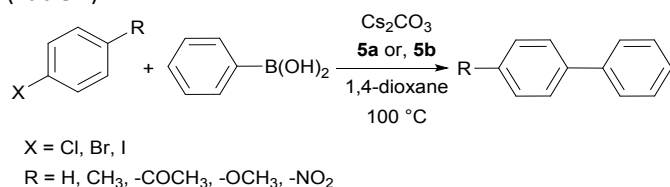
Scheme 5. Suzuki coupling reaction between aryl halides and phenylboronic acid

The bidentate macrocyclic-*trans*-bis(NHC)PdCl₂ complexes **5a** and **5b** were demonstrated to be competent precatalysts for Suzuki cross-coupling reactions. Various aryl halides, including aryl chlorides, bromides and iodides, were coupled with phenyl boronic acid in moderate to excellent yields (Table 1).

Table 1 Suzuki coupling of aryl halides with phenylboronic acid using (**5a-5b**)

Entry	Substrate	Time (h)	Cat.	Yield (%)[a]
1.	4-bromonitrobenzene	3	**5a**	>99
2.	4-bromonitrobenzene	3	**5b**	>99
3.	bromobenzene	3	**5a**	61
4.	bromobenzene	3	**5b**	50
5.	bromobenzene	6	**5a**	96
6.	4-iodoanisole	16	**5a**	96
7.	4-iodoanisole	10	**5b**	>99
8.	4-bromotoluene	3	**5a**	97
9.	4-bromotoluene	3	**5b**	70
10.	4-chlorotoluene	24	**5a**	37
11.	4-chlorotoluene	24	**5b**	9
12.	4-chloroacetophenone	8	**5a**	52
13.	4-chloroacetophenone	8	**5b**	>99
14.	4-chloroacetophenone	17	**5a**	70
15.	4-bromoacetophenone	3	**5a**	>99
16.	4-bromoacetophenone	3	**5b**	>99
17.	4-bromotoluene	7	**5a**	64[b]
18.	4-bromonitrobenzene	7	**5b**	9[b]
19.	4-bromonitrobenzene	7	**5a**	4[b]
20.	4-bromonitrobenzene	24	none	0

[a]The average of two runs determined by ^{1}H NMR using an internal standard. No increase in yield was observed if the reaction time was increased. Conditions: 1 mol % of precatalyst, Cs₂CO₃ (0.90 mmol), substrate (0.20 mmol), phenylboronic acid (0.45 mmol) and 1,4-dioxane (1.5 mL) at 100 °C under N₂. [b]Precatalyst loading: 0.1 mol %.

Precatalysts **5a** and **5b** both facilitate coupling of the less reactive unactivated aryl chlorides with phenylboronic acid (Table 1, Entries 10, 11) in low to moderate yields. Activated aryl-chlorides show moderate to excellent yields (Table 1, Entries 12-14). In these data, **5a** and **5b** exhibit higher activity

than similar reported non-macrocyclic catalysts.[18] Due to the apparently quantitative coupling of aryl bromides using precatalyst **5a** and **5b**, the couplings of 4-bromonitrobenzene and 4-bromotoluene with phenylboronic acid were selected for further investigations at lower precatalyst loads (0.1 mol %). At 0.1 mol % precatalyst loading, 4-bromotoluene was found to afford appreciable yield (Table 1, Entry 17) but 4-bromonitrobenzene gave poor yield (Table 1, Entries 18-19).

Next, the macrocyclic-*trans*-bis(NHC)PdCl₂ complexes were screened as precatalysts for the Heck coupling reaction (Scheme 6). Initially, 4-iodoacetophenone was combined with *n*-butyl acrylate in the presence of 0.1 to 0.02 mol % of precatalysts **5a** and **5b**.

X = Cl, Br, I

R = H, CH₃, -COCH₃, -OCH₃, -NO₂
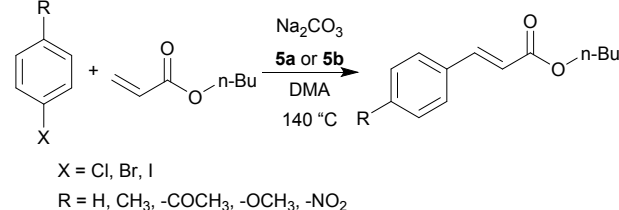
Scheme 6. Heck coupling reaction between aryl halides and n-butyl acrylate

Our data shows that **5b** generates a more active catalyst than **5a,** showing 10-16% higher yields for the Heck coupling reaction (Table 2). A possible explanation for this observation could be the absence of vinylic imidazole protons on the benzimidazole heterocycle. Imidazole C-H protons have been postulated to be acidic enough to react with bases during catalysis and serve as an additional route to catalyst decomposition.[72]

Table 2. Heck reaction between n-butyl acrylate and 4-iodoacetophenone

Entry	Cat. (mol%)	time (h)	Yield (%)[a]	TOF[b]
1.	**5a** (0.1)	1	50	510
2.	**5a** (0.1)	1.5	60	400
3.	**5a** (0.1)	4	70	670
4.	**5a** (0.02)	1	38	2037
5.	**5b** (0.1)	1	66	660
6.	**5b** (0.1)	1.5	85	567
7.	**5b** (0.1)	4	82	1025
8.	**5b** (0.02)	1	46	2378

[a]Yield determined by ^{1}H NMR using an internal standard; only the trans isomer was observed. [b]Turnover frequency (TOF) = (mol of product)/((mol of Pd) h). Conditions: All reactions used 4-iodoacetophenone (0.2 mmol), Na₂CO₃ (0.24 mmol), *tetra-n*-butylammonium bromide (0.02 mmol), *n*-butyl acrylate (0.4 mmol, 2 equivalents), dimethyl-acetamide (1.5 mL), 140 °C.

Table 3 summarizes a survey of substrates for the coupling of aryl halides with n-butyl acrylate in the presence of precatalyst **5b** (Scheme 6). Various aryl iodides and aryl bromides can be coupled with n-butyl acrylate efficiently using **5b**; however, in contrast to the Suzuki coupling reaction, aryl chlorides show low reactivity.

The Heck coupling reaction using 0.1 mol % of precatalyst **5b** shows high yield with *trans* selectivity for 4-bromonitrobenzene (Table 3, Entry 1). 4-Bromobenzene appears sluggish compared to 4-bromoacetophenone, but still gives moderate yield at longer reaction times using 0.1 mol % precatalyst (Table 3, Entries 2-5). 4-Bromoacetophenone affords a yield of 32 % using

0.02 mol % **5b,** which is comparable to literature reports at similar catalyst loadings.[32] 4-Chlorotoluene does not show appreciable yield of product, and 4-chloroacetophenone only shows low yield at 0.1 mol % precatalyst (Table 3, Entries 7-8). Overall, precatalysts **5a** and **5b** show comparable catalytic performance for the Heck reaction with a broader substrate scope than similar macrocyclic Pd(II) systems reported in the literature.[36] We must note that the performance of **5a** and **5b** is poor when compared to state-of-the-art Pd C-C coupling systems. State-of-the-art systems currently can afford near complete conversion at catalyst loadings of 100 mol ppm or lower. Additionally, some reports of TOF values are several orders of magnitude greater than those found here.[73] Other analogous compounds in the literature also show poor performance compared to state-of-the-art systems.[18,36]

The competence of complexes **5a** and **5b** as precatalysts for C-C bond forming reactions implies that an active molecular catalyst species could be capable of facile *cis* / *trans* isomerization of the NHC moieties through intramolecular five-coordinate rearrangement assisted by the pendant amines present in the macrocycle (Scheme 7).[74]

Table 3 Heck coupling of aryl halides with n-butyl acrylate using **5b**

Entry	substrate	mol%	time (h)	Yield (%)[a]
1.	4-bromonitrobenzene	0.1	4	>99
2.	4-bromoacetophenone	0.1	1	51
3.	4-bromoacetophenone	0.02	1	32
4.	4-bromotoluene	0.1	7	47
5.	bromobenzene	0.1	8	42
6.	4-iodoanisole	0.1	1	50
7.	4-chlorotoluene	0.1	16	0
8.	4-chlomoacetophenone	0.1	16	4
9.	4-bromonitrobenzene	none	24	0

[a]Yield determined by ^{1}H NMR using an internal standard. Only the trans isomers were observed. Conditions: All reactions used 0.1 mol % of precatalyst **5a** and **5b**, aryl halide (0.2 mmol), Na_2CO_3 (0.24 mmol), tetra-n-butylammonium bromide (0.02 mmol), n-butyl acrylate (0.4 mmol, 2 equivalents), dimethylacetamide (1.5 mL), 140 ˚C.

The formation of colloidal palladium clusters that serve as a reservoir for the actual catalytic species is common in Pd catalysis.[75-77] Douthwaite and co-workers reported the possibility of ligand de-coordination from the metal during a catalytic reaction and concluded that the reaction might be catalyzed by colloidal palladium because they observed an increase in turnover frequency at lower catalyst loading. In this work, **5a** and **5b** also show an increase in activity at lower catalyst loading, which is a common feature of Pd[0] catalyzed reactions.[32] This observation is inconsistent with the previous report of similar Pd systems,[18] and we infer that loss of ligand from the metal and formation of colloidal Pd is indeed possible. Recent work by Ananikov demonstrates that Pd-based "cocktail systems" in fact contain several dominant catalytic species.[78] Furthermore, studies have shown that the popular Hg drop test in fact seems to be deficient in distinguishing between possible catalytic species.[79] Further detailed mechanistic studies are underway and will be reported elsewhere. These Pd systems are our first step into exploring the coordination chemistry and

reactivity of these macrocyclic ligands; to combat ligand de-coordination, we plan to explore metals that will favour κ[3] and higher coordination numbers for the macrocyclic ligands.
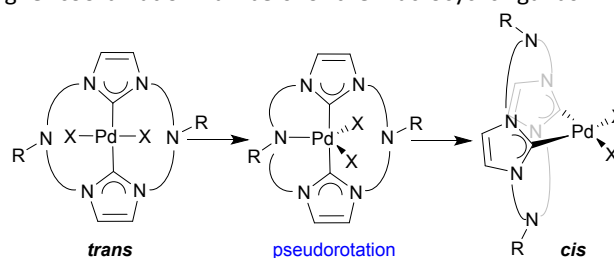
Scheme 7. cis / trans isomerisation promoted by pendant amine groups via 5-coordinate rearrangement.

Conclusions

In conclusion, we have synthesized 20-membered macrocyclic bis(NHC)-imidazolium proligands **3a** and **3b** derived from imidazole and benzimidazole, Ag complexes **4a** and **4b,** and novel macrocyclic-*trans*-bis(NHC)Pd(II)Cl$_2$ complexes **5a** and **5b**. Interestingly, solid-state samples of **4a** and **4b** are dimeric and show different coordination environments for the Ag(I)-anionic core of dimeric structures. Ag complexes **4a** and **4b** were competent transmetalation agents to bis(acetonitrile)-dichloropalladium(II). Complexes **5a** and **5b** were found to be stable towards air, moisture and heat. The molecular structures of proligand **3a** and **3b**, Ag carbene complexes **4a** and **4b,** and macrocyclic-*trans*-bis(NHC)Pd(II)Cl$_2$ complexes **5a** and **5b** were determined by single-crystal X-ray crystallography. **5a** and **5b** possess a square-planar metal center, and the 20-membered macrocyclic-bis(NHC)-imidazolium/benzimidazolium moiety acts as a bidentate ligand. The coordination modes of the ligand have been observed to consistently be κ[2] in the solid state and at no point is formation of cationic metal complexes by displacement of an inner-sphere halide observed. Additionally, *cis* / *trans* mixtures of the NHC moieties are not observed in the solid state for the Pd systems synthesized. The exploration of the transmetalation behaviour of **4a** and **4b** with other metals and the resultant coordination geometries of these macrocyclic ligands will be reported elsewhere.

The macrocyclic-*trans*-bis(NHC)palladium(II) complexes **5a** and **5b** were demonstrated to be active precatalysts for Heck and Suzuki cross-coupling reactions. Unactivated aryl-Cl bonds can undergo Suzuki coupling in modest yield by **5a.** Notably, we observed near quantitative yield for Suzuki coupling of the activated substrate 4-chloroacetophenone catalyzed by **5b.** This result is comparable to state-of-the-art catalyst systems capable of coupling aryl-Cl bonds, which are generally considered to be less reactive than heavier aryl halides.[80] We have shown that complexes **5a** and **5b** can catalyze Suzuki and Heck coupling reactions in the presence of the steric bulk of our macrocyclic ligands encompassing the Pd center. Although our catalysts are not as active as current state-of-the-art Pd coupling systems, our results show improved yield at shorter reaction times compared to macrocyclic and analogous Pd compounds in the literature.[36,18]

Experimental Methods

General Procedures

Oxygen- and water-sensitive reactions and manipulations were performed using glove box and Schlenk techniques under nitrogen atmosphere. All solvents were purchased anhydrous and were stored over molecular sieves in the glove box. All reagents were used as supplied (Aldrich). [PdCl$_2$(MeCN)$_2$] was prepared[81] using the literature procedure. High-resolution mass spectra were recorded using a Bruker APEX-II FTMS instrument with an electrospray ionization source. Standard ESI-MS spectra were recorded on a Shimadzu 8040 triple quadrupole-MS system. X-ray crystallographic data were collected on a Bruker APEX CCD-based X-ray diffractometer. ^{1}H and ^{13}C NMR spectra were recorded at probe temperature on 300 MHz and Bruker Avance DPX 400 spectrometers. Chemical shifts are reported in parts per million downfield shift from SiMe$_4$; coupling constants are reported in Hz. ^{1}H NMR spectra were referenced internally to the residual proton solvent resonance of CDCl$_3$ (δ 7.26), CD$_2$Cl$_2$ (δ 5.32), DMSO-d_6 (δ 2.50). ^{13}C NMR spectra were referenced to CDCl$_3$ (δ 77.0), CH$_2$Cl$_2$ (δ 53.84), DMSO-d_6 (δ 39.51). ^{1}H COSY, ^{13}C HSQC, NOESY experiments were performed using standard Bruker pulse sequences. Microanalysis were performed by Midwest Microlab (Indianapolis, Indiana) or at the University of Rochester CENTC facility where microanalysis samples were weighed with a PerkinElmer Model AD-6 Autobalance and their compositions were determined with a PerkinElmer 2400 Series II Analyzer. Air-sensitive samples were handled in a VAC Atmospheres glovebox at the CENTC facility. Gas chromatography was performed on an Agilent 6890/5973N in positive ion CI mode with a flow rate of 1 mL/min constant flow He, inlet temperature of 250°C, column temperature of 80°C, 20°C/min increase to 250°C (held for 2 min) for a total time of 16 min.

X-ray crystallography

A crystal of suitable shape and dimensions was selected for structural analysis. Intensity data were collected using a diffractometer with a Bruker APEX CCD area detector[82] and graphite-monochromated radiation. The data were corrected for absorption by the empirical method,[83] giving minimum and maximum transmission factors. The space group was determined by systematic absences and statistical tests and was verified by subsequent refinement. The structure was solved by direct methods and was refined by full-matrix least-squares methods[84] on F^2. The positions of hydrogens bonded to carbons were initially determined by geometry and were refined using a riding model. Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atom displacement parameters were set to 1.2 times the isotropic equivalent displacement parameters of the bonded atoms. A summary of refinement parameters can be found in Table 4. Further description and details of the refinement of each structure can be found in the supporting information.

Synthesis and Characterization of Compounds.

Compounds **A**, **B** and **1** were synthesized according to literature procedures.[5,6]

N-benzylbis(3-imidazolpropyl)amine (2a).

Imidazole (0.86 g, 12.6 mmol) in THF (10 mL) was added dropwise to NaH (0.30 g, 12.6 mmol) while stirring at ambient temperature. Stirring was continued for 16 hours. To this slurry, N-benzylbis(3-bromopropyl)amine (1.2 g, 3.44 mmol) in THF (10 mL) solution was added, and the resulting solution was stirred for an additional 16 hours. The solution was filtered and the volatile material was removed under reduced pressure to yield N-benzylbis(3-imidazolpropyl)amine as an pale yellow viscous liquid (1.76 g, 95 %). ^{1}H NMR (CDCl$_3$): δ 7.37-7.02 (m, 5H of C$_6$H$_5$), 7.02 (s, 2H, imi), 6.78 (s, 2H, imi), 3.94 (t, J = 6.72, 4H, -NCH_2), 3.52 (s, 2H, PhCH_2), 2.42 (t, J = 4H), 1.87 (pen, J = 6.72, 4H). ^{13}C NMR (CDCl$_3$): δ 139, 137.1, 129.5, 128.8, 128.5, 127.4, 118.6, 58.7, 50.8, 44.6, 28.6. HR FT-ICR MS calcd for [C$_{19}$H$_{25}$N$_5$+H]: m/z [M+H]$^+$: 324.2183; found 324.2803.

N-benzylbis(3-benzimidazolpropyl)amine (2b).

Benzimidazole (0.75 g, 6.30 mmol) in THF (10 mL) was added dropwise to NaH (151 mg, 6.30 mmol) while stirring at ambient temperature. Stirring was continued for 16 hours. To this slurry, N-benzylbis(3-bromopropyl)amine (1 g, 2.86 mmol) was added and the resulting solution was stirred for an additional 16 hours. The solution was filtered, and the volatile material was removed under reduced pressure to yield N-benzylbis(3-benzimidazol-propyl)amine as an colorless viscous liquid (1.13 g, 94 %). ^{1}H NMR (CDCl$_3$): δ 7.82-7.78 (ortho, 2H of –CH$_2$C$_6$H$_5$), 7.58 (s, 2H, benzimi-NCHN-), 7.34-7.27 (m, 8H, benzimi and 3H, -CH$_2$C$_6$H$_5$), 4.12 (t, J = 6.8, 4H, -NCH_2), 3.52 (s, 2H, PhCH_2), 2.42 (t, J = 6.4, 4H), 1.87 (pen, J = 6.8, 4H, PhCH$_2$CH_2CH$_2$). ^{13}C NMR (CDCl$_3$): δ 144, 143, 139, 133.7, 129, 128.7, 127.6, 122.9, 122.2, 120.6, 109.6, 58.7, 51.2, 43, 27. HR FT-ICR MS calcd for C$_{27}$H$_{29}$N$_5$): m/z [M+H]$^+$: 424.2183; found 424.2496.

[L1][Br$_2$] (3a).

A solution of *N*-benzylbis(3-imidazolpropyl) amine **2a** (1.1 g, 3.4 mmol) and N-benzylbis(3-bromopropyl)amine (1 g, 2.9 mmol) in acetonitrile (200 mL) was refluxed for 48 hours. Removal of the solvent and dissolving in CHCl$_3$ at -40 ˚C gave the desired cyclic diimidazolium bromide salt **3a** as a white hygroscopic powder in 60 % yield (1.3 g). ^{1}H NMR (CD$_2$Cl$_2$): δ 10.77 (s, 2H of –NCHN-), 7.40-7.32 (m, 10H, -C$_6$H$_5$ and 4H, J = 1.5, imi-CH=CH), 4.32 (t, J = 9.20, 8H, -NCH_2), 3.59 (s, 4H, PhCH_2), 2.57 (t, J = 8.8, 8H, PhCH_2CH$_2$CH_2), 2.18 (pen, J = 9.20, 8H, PhCH$_2$CH_2CH$_2$). ^{1}H NMR (DMSO-d_6): δ 9.20 (s, 2H of –NCHN-), 7.77 (d, 4H, J = 1.5, imi-CH=CH), 7.32 (m, 10H, -C$_6$H$_5$), 4.08 (t, J = 6.90, 8H, -NCH_2), 3.51 (s, 4H, PhCH_2), 2.25 (t, J = 6.6, 8H, PhCH_2CH$_2$CH_2), 1.85 (pen, J = 7.10, 8H, PhCH$_2$CH_2CH$_2$). ^{13}C NMR (CD$_2$Cl$_2$): δ 139, 137, 129.4, 128., 127, 122, 59, 50, 48, 27. HR FT-ICR MS calcd for [C$_{32}$H$_{44}$N$_6$B$_r$)$^+$]: m/z [M-Br]$^+$: 591.2805; found 591.2803. Calcd for [C$_{32}$H$_{43}$N$_6$)$^+$]: m/z [M-2Br]$^+$: 511.3544; found 511.3546.

[L2][Br$_2$] (3b).

A solution of *N*-benzylbis(3-imidazolpropyl)amine **2b** (1 g, 2.36 mmol) and N-benzylbis(3-bromopropyl)amine (823 mg, 2.36 mmol) in acetonitrile (120 mL) was refluxed for 24 hours. Concentration of the solution and cooling to -40 ˚C gave the desired cyclophane bis(NHC) ligand **3b** as a white powder in 50 % yield (910 mg). ^{1}H NMR (CDCl$_3$): δ 11.31 (s, 2H of –NCHN-),

7.57-7.54 (d, 4H, -CH$_2$C$_6$H$_5$), 7.46 (d, 4H, benzimidazole -C$_6$H$_4$), 7.35 (t, J = 7.32, 4H, -CH$_2$C$_6$H$_5$), 7.27 (d, 4H, -CH$_2$C$_6$H$_5$), 4.64 (t, J = 7.2, 8H, benzimidazole -NCH$_2$), 3.69 (s, 4H, PhCH$_2$), 2.83 (t, J = 6.4, 8H, PhCH$_2$CH$_2$CH$_2$), 2.65 (pen, J = 7.2, 8H, PhCH$_2$CH$_2$CH$_2$). ^{13}C NMR (CDCl$_3$): δ 144 (−NCHN-), 139.5, 131.7, 129, 128.6, 127, 126, 113, 60.4 (4H, PhCH$_2$), 51.6, 45.7, 27. HR FT-ICR MS calcd for C$_{40}$H$_{48}$BrN$_6$$^+$: m/z [M-Br+H]: 693.3101, 691.3208; found 691.3118, 693.3099. Anal. Found for C$_{40}$H$_{48}$Br$_2$N$_6$: C 62.33, H 6.21, N 11.052%; Calcd, C 62.18, H 6.26, N 10.88%.

Generation of free carbene *in situ* (3c).

A grey suspension of sodium hydride (25 mg, 0.037 mmol) in 1 mL of DMSO-d_6 was added to **3a** (22 mg, 0.91 mmol) at room temperature. The reaction mixture turned red in color and effervesced immediately. The reaction mixture was stirred for 2 minutes. The reaction mixture was filtered and transferred to a J. Young tube. ^{1}H NMR (DMSO-d_6): δ 9.20 (s, 2H of −NCHN-), 7.33-7.23 (m, 10H, -C$_6$H$_5$), 3.81 (m, 8H, -NCH$_2$), 3.51 (s, 4H, PhCH$_2$), 2.27 (m, 8H, PhCH$_2$CH$_2$CH$_2$), 1.71 (m, 8H, PhCH$_2$CH$_2$CH$_2$). ^{13}C NMR (DMSO-d_6): δ 208.4, 140.0, 128.5, 128.0, 126.1, 119.0, 58.0, 50.2, 48.0, 28.0.

[(L1)Ag]$_2$(Ag$_2$Br$_4$) (4a).

3a (218 mg, 0.32 mmol) was dissolved in dichloromethane (20 mL), and Ag$_2$O (150 mg, 0.64 mmol) was added. The reaction vessel was covered with aluminium foil, and the mixture was stirred for 24 hours. The reaction mixture was then filtered through Celite, and the filtrate was dried under reduced pressure to give **4a** as a white solid. Yield: 247 mg, 86 %. Crystals suitable for X-ray diffraction studies were grown at room temperature under nitrogen by slow diffusion of pentane into the saturated dichloromethane solution of **4a**. ^{1}H NMR (CD$_2$Cl$_2$): δ 7.40 -7.25 (m, 10H, -C$_6$H$_5$), 7.05 (s, 4H, imi-CH=CH), 4.25 (t, J = 6, 8H, -NCH$_2$), 3.63 (s, 4H, PhCH$_2$), 2.62 (t, J = 5.4, 8H, PhCH$_2$CH$_2$CH$_2$), 1.96 (pen, J = 11.4, 8H, PhCH$_2$CH$_2$CH$_2$). ^{1}H NMR (CDCl$_3$): δ 7.36 (m, 10H, -C$_6$H$_5$), 7.02 (s, 4H, imi-CH=CH), 4.28 (t, J = 6, 8H, -NCH$_2$), 3.60 (s, 4H, PhCH$_2$), 2.60 (t, J = 5.2, 8H, PhCH$_2$CH$_2$CH$_2$), 1.94 (pen, J = 11.4, 8H, PhCH$_2$CH$_2$CH$_2$). ^{13}C NMR (CD$_2$Cl$_2$): δ 180, 139.7, 129.5, 128.5, 128.3, 126.9, 121.4, 58.2 (PhCH$_2$N), 48.6, 30.1. ^{13}C NMR (CDCl$_3$): δ 181, 139, 129, 127, 121, 59 (PhCH$_2$N), 53, 49, 30. ESI-MS calcd for [C$_{32}$H$_{42}$AgN$_6$]$^+$: m/z (M-AgBr$_2$) 617.2516; found 617.2. Calcd for [C$_{32}$H$_{42}$N$_6$+H]$^+$: (M-2AgBr+H) 511.3549; found 511.3. Anal. Found for C$_{32}$H$_{42}$Ag$_2$Br$_2$N$_6$.: C, 43.09; H, 4.75; N, 9.12%. Calcd for C$_{32}$H$_{42}$Ag$_2$Br$_2$N$_6$: C 43.36, H 4.78, N 9.48%.

[(L2)Ag]$_2$(AgBr$_2$)$_2$ (4b).

3b (100 mg, 0.13 mmol) was dissolved in dichloromethane (20 mL), and Ag$_2$O (60 mg, 0.26 mmol) was added. The reaction vessel was covered with aluminium foil, and the mixture was stirred for 24 hours. The reaction mixture was then filtered through Celite, and the filtrate was dried under reduced pressure to give **4b** as a white solid. Yield: 116 mg, 91 %. Crystals suitable for X-ray diffraction studies were grown at room temperature under nitrogen by slow diffusion of pentane into the saturated dichloromethane solution of **4b**. ^{1}H NMR (CD$_2$Cl$_2$): 7.50-7.39 (m, 8H, -CH$_2$C$_6$H$_5$ and 8H, benzimidazole -C$_6$H$_4$), 7.29 (d, 2H, para-C$_6$H$_5$), 4.72 (m, 8H, benzimidazole-NCH$_2$), 3.72 (s, 4H, PhCH$_2$), 2.73 (t, J = 4.80, 8H, PhCH$_2$CH$_2$CH$_2$), 2.05 (m, 8H, PhCH$_2$CH$_2$CH$_2$). ^{13}C NMR (CD$_2$Cl$_2$): δ 181, 144, 140, 134, 129,

128.8, 127, 124, 119, 58.6, 54.3, 46.3, 28.5. HR FT-ICR MS calcd for [C$_{40}$H$_{46}$AgN$_6$]$^+$: m/z [M-AgBr$_2$] 717.2829, 719.2828; found 717.2829, 719.2828. Calcd for [C$_{40}$H$_{46}$N$_6$+H]$^+$: m/z (M-2AgBr) 611.3857; found 611.3857. Anal. Found for C$_{40}$H$_{46}$Ag$_2$Br$_2$N$_6$(0.6C$_5$H$_{12}$): C 50.46, H 4.94, N 8.52%; Calcd, C 50.16, H 5.21, N 8.16%. Analysis was attempted several times and the best analysis obtained matched the above results with solvent remaining in the bulk solid.

trans-bis(NHC)Pd(II)Cl$_2$ (5a).

Silver carbene **4a** (210 mg, 0.237 mmol) was dissolved in dichloromethane (15 mL) and PdCl$_2$(MeCN)$_2$ (61.5 mg, 0.237 mmol) was added. The reaction was stirred at 25 ˚C for 30 minutes and at 60 ˚C for 20 hours. A pale yellow precipitate formed. The solution was cooled to room temperature and filtered, and the volatiles were removed from the filtrate under reduced pressure to give a white solid. Crude white solid was dissolved in a minimal amount of methylene chloride and excess pentane was added to precipitate the product. The product was isolated by filtration and was washed with excess pentane to give **5a** as white solid. Yield: 90 mg, 55 %. Crystals suitable for X-ray diffraction were grown at room temperature under nitrogen by slow vapor diffusion of pentane into a saturated dichloromethane solution of **5a**. ^{1}H NMR (CD$_2$Cl$_2$): 7.47 (d, J = 7.6, 4H, ortho-C$_6$H$_5$), 7.35 (t, J = 7.6, 4H, meta-C$_6$H$_5$), 7.23 (t, J = 7.2, 2H, para-C$_6$H$_5$), 6.82 (s, 4H, imidazole –CHCH-), 4.59 (t, J = 5.6, 8H, imidazole-NCH$_2$), 3.68 (s, 4H, PhCH$_2$), 3.00 (t, J = 5.6, 8H, PhCH$_2$CH$_2$CH$_2$), 2.18 (t, J = 6, 8H, PhCH$_2$CH$_2$CH$_2$). ^{13}C NMR (CD$_2$Cl$_2$): δ 170.7, 141, 129, 128.6, 127, 121, 59.8, 33.8, 47.8, 31. HR FT-ICR MS calcd for [C$_{32}$H$_{42}$ClN$_6$Pd]$^+$): m/z [M-Cl] 651.2194; found 651.2186. Anal. found for C$_{32}$H$_{42}$Cl$_2$N$_6$Pd·(CH$_2$Cl$_2$): C 51.62, H 5.36, N 10.52%;. Calcd, C 51.28, H 5.74, N 10.87 %. Analysis was attempted several times and the best analysis obtained matched the above results with solvent remaining in the bulk solid.

trans-bis(NHC)Pd(II)X$_2$ (5b).

Silver carbene **4b** (150 mg, 0.152 mmol) was dissolved in dichloromethane (10 mL), and PdCl$_2$(MeCN)$_2$ (40 mg, 0.155 mmol) was added. The reaction was stirred at 25 ˚C for 30 minutes and at 60 ˚C for 20 hours. A pale yellow precipitate formed. The solution was cooled to room temperature and filtered, and the volatiles were removed from the filtrate under reduced pressure and were washed with pentane to give **5b** as a white solid. Yield: 72 mg, 58 % based on C$_{40}$H$_{46}$N$_6$PdCl$_{1.47}$Br$_{0.43}$ (MW = 807.24). Crystals suitable for X-ray diffraction were grown at room temperature under nitrogen by slow vapor diffusion of pentane into a saturated dichloromethane solution of 5b. ^{1}H NMR (CD$_2$Cl$_2$): δ 7.56 -7.25 (m, aromatic 18H, -C$_6$H$_5$ and 4H, imi-CH=CH), 5.02 (bs, 8H, benzimidazole-NCH$_2$), 3.76 (s, 4H, PhCH$_2$), 3.09 (bs, 8H, PhCH$_2$CH$_2$CH$_2$), 2.18 (t, J = 5.6, 8H, PhCH$_2$CH$_2$CH$_2$). ^{13}C NMR (CD$_2$Cl$_2$): δ 182.6, 141.2, 134.8, 128.9, 128.7, 127, 123, 110, 59, 44.5, 30.1, 28.7. HR FT-ICR MS calcd for [C$_{40}$H$_{46}$Cl$_2$N$_6$Pd]$^+$): m/z [M-Cl] 751.2507; found 751.2518. Anal. found for C$_{40}$H$_{46}$Cl$_{1.57}$Br$_{0.43}$N$_6$Pd·(CH$_2$Cl$_2$): C 55.19, H 5.42, N 9.42%; Calcd, C 55.39, H 5.47, N 9.40%. Analysis was attempted several times and the best analysis obtained matched the above results with solvent remaining in the bulk solid.

General procedure for Suzuki coupling reactions.

A 15 mL Teflon-sealed pressure tube with a magnetic stir bar was charged with aryl halide (0.2 mmol), phenylboronic acid (36 mg, 0.45 mmol), cesium carbonate (196 mg, 0.90 mmol), and 1,3,5-trimethoxybenzene (20-30 mg) as an internal standard. Then, 1,4-dioxane (1.50 mL) and a solution of the precatalyst in CH_2Cl_2 (0.1 mol %, 50 μL, 0.04 M) were added in the glove box. The reaction mixture was heated to 100 °C in an oil bath with vigorous stirring. The reaction mixture was filtered through a short pad of SiO_2, and the filtrate was analyzed by GC and ^1H NMR.

General procedure for Heck coupling reactions.

A 15 mL Teflon-sealed pressure tube with a magnetic stir bar was charged with aryl halide (0.20 mmol), n-butyl acrylate (51.3 mg, 0.40 mmol), n-butyl ammonium bromide (6.5 mg, 0.02 mmol), and 1,3,5-trimethoxybenzene (20-30 mg) as an internal standard. A solution of precatalyst (0.02 mol %, 50 μL, 4 mM solution) in CH_2Cl_2 was added in the glove box. Anhydrous Na_2CO_3 (24 mg, 0.23 mmol) and N,N-dimethylacetamide (2 mL) were added, and the tube was flushed with N_2. The reaction mixture was heated in an oil bath at 140 °C for the desired time period. The reaction mixture was cooled and filtered through a short pad of SiO_2. The filtrate was analyzed by ^1H NMR.

Conflicts of interest

The authors declare no conflicts of interest.

Table 4. Crystal data and structure refinement for silver carbene complexes **4a, 4b** , **5a** and **5b**

	3a	4a	4b	5a	5b
Empirical formula	$C_{34}H_{46}Br_2Cl_6N_6$	$C_{65}H_{86}Ag_4Br_4Cl_2N_{12}$	$C_{82}H_{96}Ag_4Br_4Cl_4N_{12}$	$C_{32}H_{42}Cl_2N_6Pd$	$C_{40}H_{46}Br_{0.43}Cl_{1.57}N_6Pd$
Formula weight	911.29	1857.47	2142.62	688.01	807.24
Crystal system	orthorhombic	monoclinic	monoclinic	monoclinic	monoclinic
Space group	*Pbca*	P2₁/c	C2/c	P2₁/c	P2₁/n
a (Å)	9.350(3)	9.840(4)	31.67(4)	11.612(4)	12.462(17)
b (Å)	16.797(6)	22.482(8)	10.719(17)	8.505(2)	10.751(15)
c (Å)	25.649(8)	15.732(6)	25.17(4)	16.280(5)	14.335(19)
α (deg)	90	90	90	90	90
β (deg)	90	93.172(5)	105.24(2)	94.685(4)	103.665(19)
γ (deg)	90	90	90	90	90
Volume (Å³)	4028(2)	3475(2)	8244(21)	1602.4(8)	1866(4)
Z, Z′	4, 0.5	2, 0.5	4, 0.5	2, 0.5	2, 0.5
Density (calcd) (Mg/m³)	1.503	1.775	1.726	1.426	1.437
Wavelength (Mg/m³)	0.71073	0.71073	0.71073	0.71073	0.71073
Temperature (K)	100(2)	100(2)	100(2)	100(2)	100(2)
F(000)	1856	1844	4272	712	831
Absorption coeff. (mm⁻¹)	2.443	3.536	3.056	0.777	1.107
Absorption correction	Semi-emp. from equiv.	Semi-emp. from equiv.	Semi-emp. from equiv.	Semi-emp. from equiv.	Semi-emp. from equiv.
Max. & min. transmission	0.775 and 0.509	0.869 and 0.373	0.3766 and 0.2313	0.812 and 0.757	0.3782 and 0.2597
θ range /°	1.588 to 27.569	1.581 to 27.723	1.333 to 22.721	1.760 to 27.581	1.950 to 22.722°
Reflection collected	149026	49788	17622	81927	14735
Independent reflection	11335 [R(int)=0.0759]	11151 [R(int)=0.0427]	5545 [R(int)=0.0990]	14455 [R(int)=0.0474]	2508 [R(int)=0.1061]
Data / restraints/ param.	11335 / 0 / 218	11151 / 321 / 380	5545 / 588 / 529	14455 / 0 / 189	2508 / 660 / 333
$wR(F^2$ all data)	wR2 = 0.1750	wR2 = 0.1415	wR2 = 0.2256	*wR2 = 0.2326*	wR2 = 0.2636
R(F obsd. data)	R1 = 0.0597	R1 = 0.0579	*R*1 = 0.0835	*R1 = 0.0751*	*R*1 = 0.0879
Goodness-of-fit on F²	1.006	1.007	1.009	1.004	1.007
Observed data [I>2 σ(I)]	7787	7804	3917	9254	1897
Largest & mean shift / s.u.	0.001, 0.000	0.001, 0.000	0.001, 0.000	0.000, 0.000	0.035, 0.003
Largest diff peak and hole e/Å³	3.282 and -0.783	2.592 and -0.912	1.485 and -1.066	3.153 and -1.415	0.779 and -0.853
τ₄				0.000	0.038

$$wR2 = \{ \Sigma\, [w(F_O^2 - F_c^2)^2] / \Sigma\, [w(F_O^2)^2] \}^{1/2} , \; R1 = \Sigma\, ||F_O| - |F_c|| / \Sigma\, |F_O|$$

Acknowledgements

References

1   Arduengo, A. J.; Harlow, R. L.; Kline, M., A stable crystalline carbene. *Journal of the American Chemical Society* **1991,** *113* (1), 361-363.

2   Kuwata, S.; Hahn, F. E., Complexes bearing protic N-heterocyclic carbene ligands. *Chemical Reviews* **2018,** *118* (19), 9642-9677.

3   Poyatos, M.; Mata, J. A.; Peris, E., Complexes with poly(N-heterocyclic carbene) ligands: structural features and catalytic applications. *Chemical Reviews* **2009,** *109* (8), 3677-3707.

4   Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F., An overview of N-heterocyclic carbenes. *Nature* **2014,** *510* (7506), 485-496.

5   Shaughnessy, K. H., Hydrophilic ligands and their application in aqueous-phase metal-catalyzed reactions. *Chemical Reviews* **2009,** *109* (2), 643-710.

6   Herrmann, W. A., N-heterocyclic carbenes: A new concept in organometallic catalysis. *Angewandte Chemie-International Edition* **2002,** *41* (8), 1290-1309.

7   Herrmann, W. A.; Goossen, L. J.; Spiegler, M., Chiral oxazoline/imidazoline-2-ylidene complexes. *Organometallics* **1998,** *17* (11), 2162-2168.

8   Douthwaite, R. E.; Green, M. L. H.; Silcock, P. J.; Gomes, P. T., Cationic and neutral palladium(II) methyl complexes of di-N-heterocyclic carbenes. *Journal of the Chemical Society-Dalton Transactions* **2002,** (7), 1386-1390.

9   Nielsen, D. J.; Cavell, K. J.; Skelton, B. W.; White, A. H., A pyridine bridged dicarbene ligand and its silver(I) and palladium(II) complexes: synthesis, structures, and catalytic applications. *Inorganica Chimica Acta* **2002,** *327*, 116-125.

10 McGuinness, D. S.; Mueller, W.; Wasserscheid, P.; Cavell, K. J.; Skelton, B. W.; White, A. H.; Englert, U., Nickel(II) heterocyclic carbene complexes as catalysts for olefin dimerization in an imidazolium chloroaluminate ionic liquid. *Organometallics* **2002,** *21* (1), 175-181.

11 Scott, N. M.; Nolan, S. P., Stabilization of organometallic species achieved by the use of N-heterocyclic carbene (NHC) ligands. *European Journal of Inorganic Chemistry* **2005,** (10), 1815-1828.

12 (a) Mata, J. A.; Poyatos, M.; Peris, E., Structural and catalytic properties of chelating bis- and tris-N-heterocyclic carbenes. *Coordination Chemistry Reviews* **2007,** *251* (5-6), 841-859. (b) Herrmann, W. A.; Schwarz, J.; Gardiner, M. G. High-yield syntheses of sterically demanding bis(N-heterocyclic carbene) complexes of palladium,. *Organometallics* **1999**, *18* (20), 4082–4089.

13 Eckhardt, M.; Fu, G. C., The first applications of carbene ligands in cross-couplings of alkyl electrophiles: Sonogashira reactions of unactivated alkyl bromides and iodides. *Journal of the American Chemical Society* **2003,** *125* (45), 13642-13643.

14 Pugh, D.; Danopoulos, A. A., Metal complexes with 'pincer'-type ligands incorporating N-heterocyclic carbene functionalities. *Coordination Chemistry Reviews* **2007,** *251* (5-6), 610-641.

15 McGuinness, D. S.; Cavell, K. J., Donor-functionalized heterocyclic carbene complexes of palladium(II): Efficient catalysts for C-C coupling reactions. *Organometallics* **2000,** *19* (5), 741-748.

16 Peris, E.; Loch, J. A.; Mata, J.; Crabtree, R. H., A Pd complex of a tridentate pincer CNC bis-carbene ligand as a robust homogenous Heck catalyst. *Chemical Communications* **2001,** (2), 201-202.

17 Hahn, F. E.; Jahnke, M. C.; Gomez-Benitez, V.; Morales-Morales, D.; Pape, T., Synthesis and catalytic activity of pincer-type bis(benzimidazolin-2-ylidene) palladium complexes. *Organometallics* **2005,** *24* (26), 6458-6463.

18 Blakemore, J. D.; Chalkley, M. J.; Farnaby, J. H.; Guard, L. M.; Hazari, N.; Incarvito, C. D.; Luzik, E. D.; Suh, H. W., New bidentate trans-chelating N-heterocyclic carbene ligands for palladium. *Organometallics* **2011,** *30* (7), 1818-1829.

19 Crabtree, R. H., NHC ligands versus cyclopentadienyls and phosphines as spectator ligands in organometallic catalysis. *Journal of Organometallic Chemistry* **2005,** *690* (24-25), 5451-5457.

20 Diez-Gonzalez, S.; Marion, N.; Nolan, S. P., N-heterocyclic carbenes in late transition metal catalysis. *Chemical Reviews* **2009,** *109* (8), 3612-3676.

21 Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G., Palladium complexes of N-heterocyclic carbenes as catalysts for cross-coupling reactions - A synthetic chemist's perspective. *Angewandte Chemie-International Edition* **2007,** *46* (16), 2768-2813.

22 Marion, N.; Nolan, S. P., Well-defined N-heterocyclic carbenes-palladium(II) precatalysts for cross-coupling reactions. *Accounts of Chemical Research* **2008,** *41* (11), 1440-1449.

23 Klawitter, I.; Anneser, M. R.; Dechert, S.; Meyer, S.; Demeshko, S.; Haslinger, S.; Pöthig, A.; Kühn, F. E.; Meyer, F. Iron Complexes of a Macrocyclic N-Heterocyclic Carbene/Pyridine Hybrid Ligand. *Organometallics* **2015**, *34* (12), 2819–2825.

24 Anneser, M. R.; Elpitiya, G. R.; Powers, X. B.; Jenkins, D. M. Toward a Porphyrin-Style NHC: A 16-Atom Ringed Dianionic Tetra-NHC Macrocycle and Its Fe(II) and Fe(III) Complexes. *Organometallics* **2019**, *38* (4), 981–987.

25 Morgan, B. P.; Galdamez, G. A.; Gilliard, R. J.; Smith, R. C., Canopied trans-chelating bis(N-heterocyclic carbene) ligand: synthesis, structure and catalysis. *Dalton Transactions* **2009,** (11), 2020-2028.

26 Nielsen, D. J.; Cavell, K. J.; Skelton, B. W.; White, A. H., Silver(I) and palladium(II) complexes of an ether-functionalized quasi-pincer bis-carbene ligand and its alkyl analogue. *Organometallics* **2006,** *25* (20), 4850-4856.

27 Alcalde, E.; Ceder, R. M.; Lopez, C.; Mesquida, N.; Muller, G.; Rodriguez, S., Coordination features of bis(N-heterocyclic carbenes) and bis(oxazolines) with 1,3-alkylidene-2,4,6-trimethylbenzene spacers. Synthesis of the ligands and silver and palladium complexes. *Dalton Transactions* **2007,** (25), 2696-2706.

28 Perry, M. C.; Cui, X. H.; Burgess, K., A modular approach to trans-chelating, N-heterocyclic carbene ligand complexes. *Tetrahedron-Asymmetry* **2002,** *13* (18), 1969-1972.

29 Chou, C. C.; Yang, C. C.; Syu, H. B.; Kuo, T. S., Monomeric Pd(II) complexes with trans-chelated pyrazole ligands as effective pre-catalysts for Heck cross-coupling reaction under mild aerobic conditions. *Journal of Organometallic Chemistry* **2013,** *745*, 387-392.

30 Clyne, D. S.; Jin, J.; Genest, E.; Gallucci, J. C.; RajanBabu, T. V., First chelated chiral N-Heterocyclic bis-carbene complexes. *Organic Letters* **2000,** *2* (8), 1125-1128.

31 Baker, M. V.; Brown, D. H.; Simpson, P. V.; Skelton, B. W.; White, A. H., Palladium complexes of o-xylyl-linked

alkoxybenzimidazolin-2-ylidenes: interesting structural conformations and application as pre-catalysts. *Dalton Transactions* **2009,** (35), 7294-7307.

32 Houghton, J.; Dyson, G.; Douthwaite, R. E.; Whitwood, A. C.; Kariuki, B. M., Structural variation, dynamics, and catalytic application of palladium(II) complexes of di-N-heterocyclic carbene-amine ligands. *Dalton Transactions* **2007,** (28), 3065-3073.

33 Douthwaite, R. E.; Houghton, J.; Kariuki, B. M., The synthesis of a di-N-heterocyclic carbene-amido complex of palladium(II). *Chemical Communications* **2004,** (6), 698-699.

34 Radloff, C.; Gong, H. Y.; Brinke, C. S. T.; Pape, T.; Lynch, V. M.; Sessler, J. L.; Hahn, F. E., Metal-dependent coordination modes displayed by macrocyclic polycarbene ligands. *Chemistry-a European Journal* **2010,** 16 (44), 13077-13081.

35 Melaiye, A.; Sun, Z. H.; Hindi, K.; Milsted, A.; Ely, D.; Reneker, D. H.; Tessier, C. A.; Youngs, W. J., Silver(I)-imidazole cyclophane gem-diol complexes encapsulated by electrospun tecophilic nanofibers: Formation of nanosilver particles and antimicrobial activity. *Journal of the American Chemical Society* **2005,** 127 (7), 2285-2291.

36 Watarai, N.; Kawasaki, H.; Azumaya, I.; Yamasaki, R.; Saito, S., Synthesis, structure and catalytic activity of macrocyclic NHC Pd pincer complexes. *Heterocycles* **2009,** 79, 531-548.

37 Meyer, K.; Dalebrook, A. F.; Wright, L. J., Selective palladation of a large (32 ring atom) macrocyclic ligand at a bis(N-heterocyclic carbene) coordination pocket through transmetallation of the corresponding mercury(II) derivative. *Dalton Transactions* **2012,** 41 (46), 14059-14067.

38 Andrew, R. E.; Chaplin, A. B., Synthesis, structure and dynamics of NHC-based palladium macrocycles. *Dalton Transactions* **2014,** 43 (3), 1413-1423.

39 Altmann, P. J.; Weiss, D. T.; Jandl, C.; Kühn, F. E. Exploring Coordination Modes: Late Transition Metal Complexes with a Methylene-Bridged Macrocyclic Tetra-NHC Ligand. *Chem. Asian J.* **2016,** 11 (10), 1597–1605.

40 Klawitter, I.; Anneser, M. R.; Dechert, S.; Meyer, S.; Demeshko, S.; Haslinger, S.; Pöthig, A.; Kühn, F. E.; Meyer, F. Iron Complexes of a Macrocyclic N-Heterocyclic Carbene/Pyridine Hybrid Ligand. *Organometallics* **2015**, 34 (12), 2819–2825.

41 (a) Bass, H. M.; Cramer, S. A.; Price, J. L.; Jenkins, D. M. 18-Atom-Ringed Macrocyclic Tetra-Imidazoliums for Preparation of Monomeric Tetra-Carbene Complexes. Organometallics 2010, 29 (15), 3235–3238. (b) Garrison, J. C.; Simons, R. S.; Talley, J. M.; Wesdemiotis, C.; Tessier, C. A.; Youngs, W. J. Synthesis and Structural Characterization of an Imidazolium-Linked Cyclophane and the Silver Complex of an N-Heterocyclic Carbene-Linked Cyclophane. Organometallics 2001, 20 (7), 1276–1278. (c) Bass, H. M.; Cramer, S. A.; McCullough, A. S.; Bernstein, K. J.; Murdock, C. R.; Jenkins, D. M. Employing Dianionic Macrocyclic Tetracarbenes To Synthesize Neutral Divalent Metal Complexes. Organometallics 2013, 32 (7), 2160–2167.

42 Weiss, D. T.; Altmann, P. J.; Haslinger, S.; Jandl, C.; Pöthig, A.; Cokoja, M.; Kühn, F. E. Structural Diversity of Late Transition Metal Complexes with Flexible Tetra-NHC Ligands. *Dalton Trans.* **2015**, 44 (42), 18329–18339.

43 (a) Weiss, D. T.; Haslinger, S.; Jandl, C.; Pöthig, A.; Cokoja, M.; Kühn, F. E. Application of Open Chain Tetraimidazolium Salts as Precursors for the Synthesis of Silver Tetra(NHC) Complexes. *Inorg. Chem.* **2015**, 54 (2), 415–417. (b) Hollering, M.; Weiss, D. T.; Bitzer, M. J.; Jandl, C.; Kühn, F. E. Controlling Coordination Geometries: Ru–Carbene Complexes with Tetra-NHC Ligands. *Inorg. Chem.* **2016**, 55 (12), 6010–6017. (c) Wagner, T.; Pöthig, A.; Augenstein, H. M. S.; Schmidt, T. D.; Kaposi, M.; Herdtweck, E.; Brütting, W.; Herrmann, W. A.; Kühn, F. E. From Simple Ligands to Complex Structures:

Structural Diversity of Silver(I) Complexes Bearing Tetradentate (alkylene Bimpy) NHC Ligands. *Organometallics* **2015**, 34 (8), 1522–1529. (d) Weiss, D. T.; Anneser, M. R.; Haslinger, S.; Pöthig, A.; Cokoja, M.; Basset, J.-M.; Kühn, F. E. NHC Versus Pyridine: How "Teeth" Change the Redox Behavior of Iron(II) Complexes. *Organometallics* **2015**, 34 (20), 5155–5166.

44 Hahn, F. E.; Rupprecht, S., Metal-chelates of medical interest .3. Tc-99m complexes with tetradentate dicatechol ligands. *Chemische Berichte* **1991,** 124 (3), 487-491.

45 de Jong, M. R.; Engbersen, J. F. J.; Huskens, J.; Reinhoudt, D. N., Cyclodextrin dimers as receptor molecules for steroid sensors. *Chemistry-a European Journal* **2000,** 6 (21), 4034-4040

46 (a) Tapu, D.; Dixon, D. A.; Roe, C. ^{13}C NMR Spectroscopy of "Arduengo-Type" Carbenes and Their Derivatives. *Chem. Rev.* **2009**, 109 (8), 3385–3407. (b) Chen, S.; Vijayaraghavan, R.; MacFarlane, D. R.; Izgorodina, E. I. Ab Initio Prediction of Proton NMR Chemical Shifts in Imidazolium Ionic Liquids. *J. Phys. Chem. B* **2013**, 117 (11), 3186–3197. And references therein.

47 Bass, H. M.; Cramer, S. A.; McCullough, A. S.; Bernstein, K. J.; Murdock, C. R.; Jenkins, D. M. Employing Dianionic Macrocyclic Tetracarbenes To Synthesize Neutral Divalent Metal Complexes. Organometallics 2013, 32 (7), 2160–2167.

48 Monticelli, M.; Tubaro, C.; Baron, M.; Basato, M.; Sgarbossa, P.; Graiff, C.; Accorsi, G.; Pell, T. P.; Wilson, D. J. D.; Barnard, P. J., Metal complexes with di(N-heterocyclic carbene) ligands bearing a rigid ortho-, meta or para-phenylene bridge. *Dalton Transactions* **2016,** 45 (23), 9540-9552.

49 Volpe, A.; Baldino, S.; Tubaro, C.; Baratta, W.; Basato, M.; Graiff, C., Dinuclear di(N-heterocyclic carbene) iridium(III) complexes as catalysts in transfer hydrogenation. *European Journal of Inorganic Chemistry* **2016,** (2), 247-251.

50 Ortiz, A. M.; Sanchez-Mendez, A.; de Jesus, E.; Flores, J. C.; Gomez-Sal, P.; Mendicuti, F., Poly(benzyl ether) dendrimers functionalized at the core with palladium bis(N-heterocyclic carbene) complexes as catalysts for the Heck coupling reaction. *Inorganic Chemistry* **2016,** 55 (3), 1304-1314.

51 Mangalum, A.; McMillen, C. D.; Tennyson, A. G., Synthesis, coordination chemistry and reactivity of transition metal complexes supported by a chelating benzimidazolylidene carboxylate ligand. *Inorganica Chimica Acta* **2015,** 426, 29-38.

52 Brinke, C. S. T.; Pape, T.; Hahn, F. E., Synthesis of polynuclear Ag(I) and Au(I) complexes from macrocyclic tetraimidazolium salts. *Dalton Transactions* **2013,** 42 (20), 7330-7337.

53 Sluijter, S. N.; Warsink, S.; Lutz, M.; Elsevier, C. J., Synthesis of palladium(0) and -(II) complexes with chelating bis(N-heterocyclic carbene) ligands and their application in semihydrogenation. *Dalton Transactions* **2013,** 42 (20), 7365-7372.

54 Lu, Z.; Cramer, S. A.; Jenkins, D. M., Exploiting a dimeric silver transmetallating reagent to synthesize macrocyclic tetracarbene complexes. *Chemical Science* **2012,** 3 (10), 3081-3087.

55 Haque, R. A.; Salman, A. W.; Budagumpi, S.; Abdullah, A. A. A.; Majid, A., Sterically tuned Ag(I)- and Pd(II)-N-heterocyclic carbene complexes of imidazol-2-ylidenes: synthesis, crystal structures, and in vitro antibacterial and anticancer studies. *Metallomics* **2013,** 5 (6), 760-769.

56 Wanniarachchi, Y. A.; Khan, M. A.; Slaughter, L. M., An unusually static, sterically hindered silver bis(N-heterocyclic carbene) complex and its use in transmetalation. *Organometallics* **2004,** 23 (25), 5881-5884.

57 Wang, H. M. J.; Lin, I. J. B., Facile synthesis of silver(I)-carbene complexes. Useful carbene transfer agents. *Organometallics* **1998,** 17 (5), 972-975.

58 Tulloch, A. A. D.; Danopoulos, A. A.; Winston, S.; Kleinhenz, S.; Eastham, G., N-Functionalised heterocyclic carbene complexes of silver. *Journal of the Chemical Society-Dalton Transactions* **2000,** (24), 4499-4506.

59 Hu, X. L.; Tang, Y. J.; Gantzel, P.; Meyer, K., Silver complexes of a novel tripodal N-heterocyclic carbene ligand: Evidence for significant metal-carbene pi-interaction. *Organometallics* **2003,** *22* (4), 612-614.

60 Dastgir, S.; Coleman, K. S.; Green, M. L. H., Heterogenised N-heterocyclic carbene complexes: synthesis, characterisation and application for hydroformylation and C-C bond formation reactions. *Dalton Transactions* **2011,** *40* (3), 661-672.

61 (a) Lee, C. K.; Vasam, C. S.; Huang, T. W.; Wang, H. M. J.; Yang, R. Y.; Lee, C. S.; Lin, I. J. B., Silver(I) N-heterocyclic carbenes with long N-alkyl chains. *Organometallics* **2006,** *25* (15), 3768-3775. (b) Wang, H. M. J.; Lin, I. J. B. Facile synthesis of silver(i)–carbene complexes. useful carbene transfer agents. *Organometallics* **1998**, *17* (5), 972–975.

62 Lee, C. K.; Lee, K. M.; Lin, I. J. B., Inorganic-organic hybrid lamella of di- and tetranuclear silver-carbene complexes. *Organometallics* **2002,** *21* (1), 10-12.

63 Chen, W. Z.; Liu, F. H., Synthesis and characterization of oligomeric and polymeric silver-imidazol-2-ylidene iodide complexes. *Journal of Organometallic Chemistry* **2003,** *673* (1-2), 5-12.

64 Ahrens, S.; Zeller, A.; Taige, M.; Strassner, T., Extension of the alkane bridge in bisNHC-palladium-dhloride complexes. Synthesis, structure, and catalytic activity. *Organometallics* **2006,** *25* (22), 5409-5415.

65 Garrison, J. C.; Youngs, W. J. Ag(I) N-heterocyclic carbene complexes: synthesis, structure, and application. *Chem. Rev.* **2005,** *105* (11), 3978–4008.

66 Herrmann, W. A.; Elison, M.; Fischer, J.; Kocher, C.; Artus, G. R. J., Metal-complexes of N-heterocyclic carbenes - a new structural principle for catalysts in homogeneous catalysis. *Angewandte Chemie-International Edition in English* **1995,** *34* (21), 2371-2374.

67 Freixa, Z.; van Leeuwen, P., Trans-chelating diphosphines, the elusive ligands! *Coordination Chemistry Reviews* **2008,** *252* (15-17), 1755-1786.

68 (a) G. Gardiner, M.; C. Ho, C.; M. Mackay, F.; S. McGuinness, D.; Tucker, M. Selective and Adaptable Access to N , N '-Asymmetrically Substituted Imidazol-2-Ylidene Bis-NHC Ligands : Pd(Ii) Complexes Featuring Wide Variation in N - Alkyl and Aryl Steric Bulk. *Dalton Transactions* **2013**, *42* (20), 7447–7457. (b) Arslan, H.; Özdemır, İ.; Vanderveer, D.; Demır, S.; Çetınkaya, B. Synthesis and Characterization of N-Heterocyclic Carbene Palladium Complex and Its Application on Direct Arylation of Benzoxazoles and Benzothiazoles with Aryl Bromides. *Journal of Coordination Chemistry* **2009**, *62* (16), 2591–2599. (c) Schultz, K. M.; Goldberg, K. I.; Gusev, D. G.; Heinekey, D. M. Synthesis, Structure, and Reactivity of Iridium NHC Pincer Complexes. *Organometallics* **2011**, *30* (6), 1429–1437.

69 Bondi, A. van der Waals volumes and radii J. *Phys. Chem.* **1964** 68 (3), 441-451

70 Miyaura, N.; Suzuki, A., Palladium-catalyzed cross-coupling reactions of organoboron compounds. *Chemical Reviews* **1995,** *95* (7), 2457-2483.

71 Smith, R. C.; Bodner, C. R.; Earl, M. J.; Sears, N. C.; Hill, N. E.; Bishop, L. M.; Sizemore, N.; Hehemann, D. T.; Bohn, J. J.; Protasiewicz, J. D., Suzuki and Heck coupling reactions mediated by palladium complexes bearing trans-spanning diphosphines. *Journal of Organometallic Chemistry* **2005,** *690* (2), 477-481.

72 Huynh, H. V.; Jothibasu, R., Syntheses and catalytic activities of Pd(II) dicarbene and hetero-dicarbene complexes. *Journal of Organometallic Chemistry* **2011,** *696* (21), 3369-3375

73 (a) Biffis, A.; Centomo, P.; Del Zotto, A.; Zecca, M. Pd Metal Catalysts for Cross-Couplings and Related Reactions in the 21st Century: A Critical Review. *Chem. Rev.* **2018**, *118* (4), 2249–2295. (b) Roy, D.; Uozumi, Y. Recent Advances in Palladium-Catalyzed Cross-Coupling Reactions at Ppm to Ppb Molar Catalyst Loadings. *Adv. Synth. Catal.* **2018**, *360* (4), 602–625.

74 Moberg, C. Stereomutation in Trigonal-Bipyramidal Systems: A Unified Picture. *Angew. Chem. Int. Ed.* **2011**, *50* (44), 10290–10292.

75 Reetz, M. T.; Lohmer, G., Propylene carbonate stabilized nanostructured palladium clusters as catalysts in Heck reactions. *Chemical Communications* **1996,** (16), 1921-1922.

76 Roucoux, A.; Schulz, J.; Patin, H., Reduced transition metal colloids: A novel family of reusable catalysts? *Chemical Reviews* **2002,** *102* (10), 3757-3778.

77 Reetz, M. T.; de Vries, J. G., Ligand-free Heck reactions using low Pd-loading. *Chemical Communications* **2004,** (14), 1559-1563.

78 Eremin, D. B.; Ananikov, V. P. Understanding active species in catalytic transformations: from molecular catalysis to nanoparticles, leaching, "cocktails" of catalysts and dynamic systems. *Coordination Chemistry Reviews* **2017**, *346*, 2–19.

79 Chernyshev, V. M.; Astakhov, A. V.; Chikunov, I. E.; Tyurin, R. V.; Eremin, D. B.; Ranny, G. S.; Khrustalev, V. N.; Ananikov, V. P. Pd and Pt catalyst poisoning in the study of reaction mechanisms: what does the mercury test mean for catalysis? *ACS Catal.* **2019**, *9* (4), 2984–2995.

80 (a) Ouyang, J.-S.; Li, Y.-F.; Huang, F.-D.; Lu, D.-D.; Liu, F.-S. The highly efficient Suzuki–Miyaura cross-coupling of (hetero)aryl chlorides and (hetero)arylboronic acids catalyzed by "bulky-yet-flexible" palladium–PEPPSI vomplexes in air. *ChemCatChem* **2018**, *10* (2), 371–375. (b) Izquierdo, F.; Zinser, C.; Minenkov, Y.; Cordes, D. B.; Slawin, A. M. Z.; Cavallo, L.; Nahra, F.; Cazin, C. S. J.; Nolan, S. P. Insights into the catalytic activity of [Pd(NHC)(Cin)Cl] (NHC=IPr, IPrCl, IPrBr) complexes in the Suzuki–Miyaura reaction. *ChemCatChem* **2018**, *10* (3), 601–611.

81 Anderson, G. K.; Lin, M., Bis(benzonitrile)dichloro complexes of palladium and platinum. *Inorganic Syntheses* **1990,** *28*, 60-63.

82 (a) Data Reduction: S*AINT* 2**007** Bruker AXS Inc., Madison, Wisconsin, USA. (b) Data Collection: A*PEX3,* 2**007,** Bruker AXS Inc., Madison, Wisconsin, USA.

83 Krause, L.; Herbst-Irmer, R.; Sheldrick, G. M.; Stalke, D., Comparison of silver and molybdenum microfocus X-ray sources for single-crystal structure determination. *Journal of Applied Crystallography* **2015,** *48*, 3-10.

84 (a) Sheldrick, G. M., Crystal structure refinement with SHELXL. *Acta Crystallographica Section C-Structural Chemistry* **2015,** *71*, 3-8. (b) Sheldrick, G. M., SHELXT - Integrated space-group and crystal-structure determination. *Acta Crystallographica a-Foundation and Advances* **2015,** *71*, 3-8.

5a

20-member macrocyclic rings containing NHCs and amines were synthesized, and their late metal coordination chemistry explored.