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Synthesis of Pd^{II} complexes bearing an enantiomerically resolved seven-membered *N*-heterocyclic carbene ligand and initial studies of their use in asymmetric Wacker-type oxidative cyclization reactions

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ABSTRACT

The development of enantiomerically resolved, axially-chiral seven-membered *N*-heterocyclic carbene (^{7}NHC) ligands for palladium is described. These ^{7}NHC ligands are derived from enatiomerically pure 2,2′-diamino-6,6′-dimethylbiphenyl, which is transformed via a synthetic sequence consisting of *ortho*-arylation, N-alkylation, and cyclization to afford seven-membered-ring amidinium salts. Synthesis of the seven-membered amidinium salts benefits from microwave irradiation, and in-situ metalation of the amidinium salts yields ^{7}NHC–Pd^{II} complexes. The chiral ^{7}NHC–Pd complexes were examined as chiral catalysts under aerobic conditions in two intramolecular oxidative amination reactions of alkenes. In one case, enantioselectivities up to 63% ee were obtained, while the other substrate underwent cyclization to afford essentially racemic products. The catalytic data compare favorably to results obtained with a Pd^{II} catalyst bearing a chiral five-membered-ring NHC ligand and, thereby, highlight the potential significance of this new class of chiral NHC ligands.

1. Introduction

Chiral monodentate *N*-heterocyclic carbenes (NHCs) have broad potential utility in asymmetric catalysis, but successful applications of such ligands remain somewhat limited.[1,2] To our knowledge, only six transformations have been reported in which chiral monodentate NHC ligands have been employed to afford enantioselectivities above 90% ee (for representative examples, see Fig. 1). The transformations include olefin metathesis,[3] 1,4-addition of arylboronic acids to enones,[4] hydrosilylation of ketones,[5] intramolecular *alpha*-arylation of amides,[6,7] copper-catalyzed conjugate addition to cycloheptenone with diethylzinc,[8] and Ni-catalyzed reductive coupling of 1,3-dienes and aldehydes with triethylsilane.[9] All of these transformations utilize five-membered-ring NHC ligands. Two strategies have been employed in the design of chiral monodentate five-membered NHCs: 'chiral relay' and the use of chiral nitrogen substituents. In the first strategy, developed by Grubbs and co-workers,[3] chirality in the *N*-heterocycle induces an asymmetric conformation of the nonsymmetrical (but achiral) nitrogen substituents (Fig. 1, ligand L^1). In the second strategy, the ligand chirality arises from the incorporation of chiral nitrogen substituents into the ligand, for example, by Buchwald–Hartwig amination of chiral cyclophanes (Fig. 1, ligand L^2)[5,4] or by amination of 1,2-diones with chiral amines (Fig. 1, ligands L^3–L^5).[6–8] Although attempts have been made to develop ligands that feature both chiral relay and chiral nitrogen substituents, only modest success has been achieved thus far.[8,10]

NHCs are excellent ligands for metal-catalyzed aerobic oxidation reactions because metal–NHC complexes are oxidatively stable.[11] NHC–Pd complexes have been employed as catalysts for aerobic oxidation of alcohols,[12] Wacker-type cyclization of *ortho*-allyl phenols,[13] and intramolecular oxidative amination of olefins (Fig. 2a, b, and c, respectively).[14] We have been interested in the development of enantioselective aerobic oxidative amination reactions of alkenes, and the use of chiral NHC ligands was a logical starting point. In connection with these efforts, we have been exploring the development and application of a new class of NHCs based upon a seven-membered heterocyclic framework (Fig. 3b).[15,16] These seven-membered NHCs (^{7}NHCs) are attractive because they feature an axially-chiral heterocyclic framework that provides an out-of-plane projection of the nitrogen substituents (Fig. 3b). This non-planarity contrasts the in-plane orientation of the nitrogen substituents in five-membered NHCs (Fig. 3a), and we reasoned that increased enantioselectivity might be achieved in asymmetric catalysis with ^{7}NHCs. We have reported that a racemic ^{7}NHC–Pd complex is an active catalyst for the intramolecular aerobic oxidative amination of *o*-crotyl tosylanilide (Fig. 2c),[14] but, at the time of this work, we had not yet succeeded in

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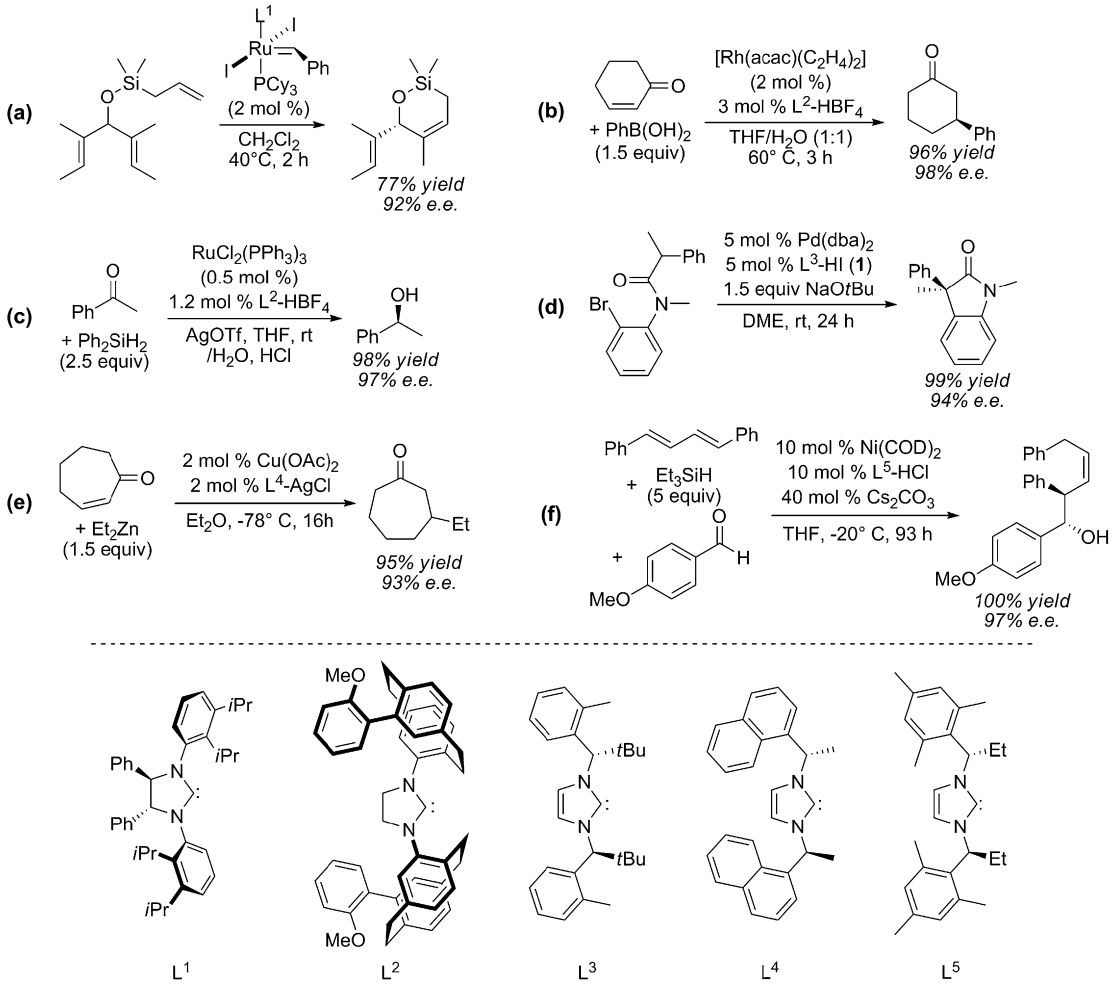


Figure 1. Asymmetric catalysis with chiral monodentate NHCs giving >90% ee.

preparing enantiomerically resolved [7]NHC–Pd complexes. Our initial synthesis of [7]NHC–Pd complexes[15] is not amenable to the synthesis of resolved analogs. Here, we describe the synthesis of enantiomerically resolved seven-membered-ring amidinium salts, metalation of the amidinium salts by Pd^{II} and the investigation of [7]NHC–Pd^{II} complexes in intramolecular aerobic oxidative heterocyclization reactions. The

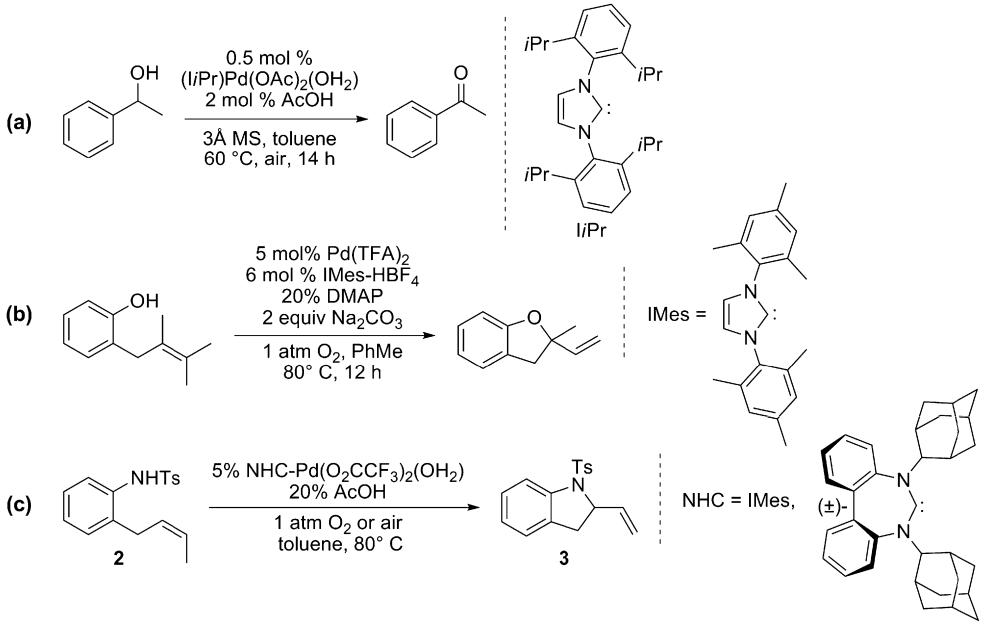


Figure 2. Palladium-catalyzed aerobic oxidation reactions that have employed NHC ligands.

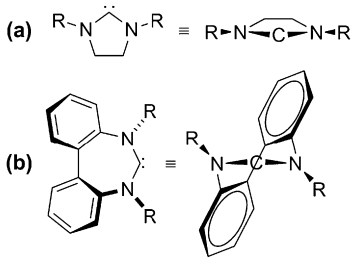


Figure 3. (a) Planarity of five-membered NHCs (^{5}NHCs). (b) Non-planarity of seven-membered NHCs (^{7}NHCs).

enantioselectivity data from the catalytic reactions is modest (≤63% ee). Nevertheless, the ^{7}NHC ligand proves to be substantially better than one of the most successful known ^{5}NHC ligands.

2. Results and discussion

2.1. Strategy

At the time this work began, there were only two reported examples of chiral monodentate ^{5}NHCs employed in reactions that achieved ee's above 90%.[3c,4] The chiral ^{5}NHCs developed by Grubbs and co-workers (L^1, Fig. 1)[3] were not useful for our goal of accessing NHC–Pd$(O_2CR)_2$ catalysts for asymmetric aerobic Wacker-type oxidation reactions because such catalysts were not synthetically accessible.[17] The chiral ^{5}NHCs developed by Andrus and co-workers (L^2, Fig. 1)[4] proved to be prohibitively difficult to synthesize. Within this context, we turned our attention to the development of new chiral NHC ligands, and our efforts led to the ^{7}NHC derivatives. After achieving preliminary success in the preparation of racemic ^{7}NHC–Pd complexes,[15] we envisioned two potential strategies to access resolved derivatives of ^{7}NHC ligands: (1) incorporation of substituents *ortho* to the nitrogens (the 3 and 3′ positions of the biphenyl moiety), and (2) use of resolved biphenyl diamines (i.e., biphenyl diamines with substituents in the 6 and 6′ positions). In the first strategy, we reasoned (and obtained preliminary support from computational modeling) that steric interactions between the *ortho* groups and the nitrogen substituents should prevent racemization of the ^{7}NHC. This strategy proved unattractive, however, because it would require independent resolution of each new amidinium salt (the ^{7}NHC-precursor).[18] We therefore focused our efforts on executing the second strategy, which would allow many resolved ^{7}NHC complexes to be synthesized from a single stock of resolved diamine.

As we have reported previously,[15a] the use of 2,2′-diamino-1,1′-binaphthyl (DABN) for the synthesis of resolved DABN-derived seven-membered-ring amidinium salts was successful only with neopentyl groups as nitrogen substituents (e.g., Fig. 4a); the corresponding amidinium salts bearing *N*-(2-adamantyl) or *N*-aryl groups were not accessible (e.g., Fig. 4b).[15,19] These observations were problematic because palladium complexes bearing ^{7}NHCs with primary nitrogen substituents proved to be unstable. The instability of ^{7}NHC–Pd complexes bearing *primary* alkyl nitrogen substituents appears to arise from decreased steric protection of the carbene carbon relative to those with *secondary* nitrogen substituents. Based on this hypothesis, we reasoned that substituents in the *ortho*-positions (i.e., the 3 and 3′ positions of the biphenyl moiety) could provide additional steric protection of the carbene carbon and, thereby, permit *primary* alkyl nitrogen substituents to be employed (Fig. 4c). Based on this proposal, we explored methods to access *ortho* substituted biaryl diamines.

2.2. Development of the Daugulis–Zaitsev *ortho*-arylation for the synthesis of *m*-quaterphenyl-2′,2″-diamines, and access to resolved ^{7}NHC–Pd complexes

Installation of steric bulk *ortho* to the nitrogen substituents of biaryl diamines required an *ortho* functionalization strategy. We recently reported that application of an *ortho* C–H arylation reaction developed by Daugulis and Zaitsev[20] provides ready access to *ortho* diarylated biaryl diamines (Scheme 1).[21] An important result from this study is that the *ortho*-arylation reaction is more effective for 2,2′-diamino-6,6′-dimethylbiphenyl (**4**) than for DABN, and we therefore turned our attention completely to the resolved diamine **4**.[22] We next examined the synthesis of $[^7NHC–H]^+$ salts derived from these new resolved quaterphenyl diamines.

This synthetic access to *ortho*-functionalized biaryl diamines enabled us to test the hypothesis that primary nitrogen substituents could be used in the preparation of stable NHC–Pd complexes. Our initial studies were carried out on the inexpensive and readily available diamine **6**, which was synthesized by acetylation, Dagulis–Zaitsev arylation, and deacetylation of 2,2′-diaminobiphenyl.[21] Sequential addition of 1-naphthaldehyde and lithium aluminum

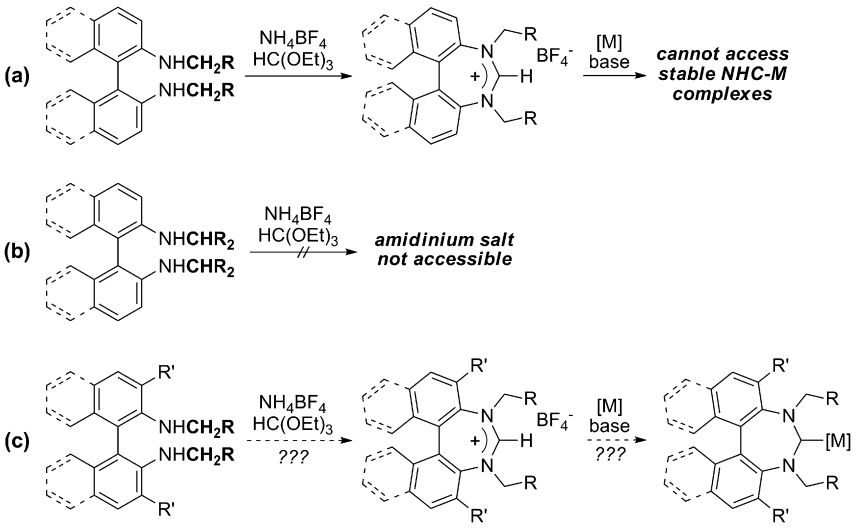
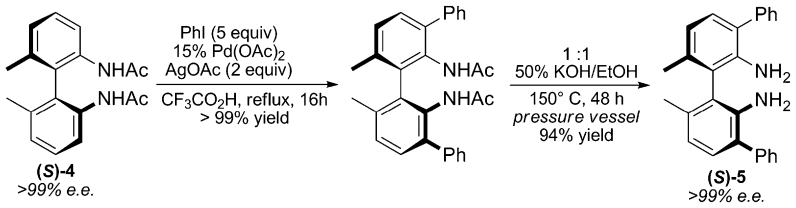
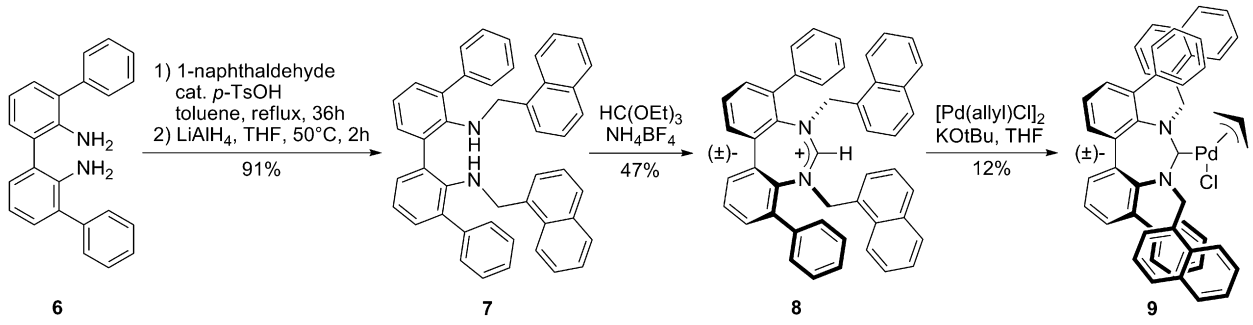


Figure 4. (a) Stable ^{7}NHC–[M] complexes are not stable with primary alkyl nitrogen substituents. (b) Resolved ^{7}NHC–HBF_4 salts are not accessible with secondary alkyl nitrogen substituents. (c) Proposed access to stable resolved ^{7}NHC–[M] complexes.



Scheme 1. Synthesis of resolved quaterphenyl diamines.



Scheme 2. Primary *N*-substituents with *ortho*-aryl groups afford a stable NHC–Pd complex.

hydride to the quaterphenyl diamine **6**[21] furnished the di-*N*-alkylated quaterphenyl diamine **7** in high yield. Cyclization of this diamine afforded the desired amidinium tetrafluoroborate salt **8**. Addition of $[Pd(allyl)Cl]_2$ and KO*t*Bu to **8** furnished the stable NHC–Pd(allyl)Cl complex **9**, albeit in low yield (Scheme 2). The structure of **9** was verified by X-ray crystallographic analysis (Fig. 5).[23] Synthesis of the stable NHC–Pd complex **9** bearing primary nitrogen substituents supported our hypothesis that incorporation of steric bulk in the *ortho*-positions of the biphenyl diamine could provide steric protection of the NHC and permit the synthesis of stable NHC–metal complexes bearing primary nitrogen substituents.

The next important challenge was to demonstrate that this synthetic approach could be used with resolved biphenyl diamines. Toward this end, **(*S*)-5** was alkylated via sequential reductive amination with cyclohexane carboxaldehyde and $LiAlH_4$ to afford **(*S*)-10** in 94% yield (Scheme 3). Initial attempts to cyclize **(*S*)-10** using published conditions[15,24] with $HC(OEt)_3$ and NH_4BF_4 to form amidinium salt **(*S*)-11** were largely unsuccessful, providing a thick dark reaction mixture after prolonged reaction times, from which only a small amount of nearly pure amidinium salt could be extracted; shorter reaction times provided very low yields as well. We ultimately found the cyclization reaction could be achieved by employing microwave irradiation.[25] The amidinium salt **(*S*)-11** was obtained in 38% yield, and workup of the crude mixture was not as challenging. Metalation of amidinium salt **(*S*)-11** with KO*t*Bu and $[Pd(allyl)Cl]_2$ afforded the ^{7}NHC–Pd(allyl)Cl complex **(*S*)-12** in 29% yield (Scheme 3). As NHC–Pd(carboxylate)$_2$ complexes are of catalytic relevance,[11,12] we sought to make such a complex from **(*S*)-12**.

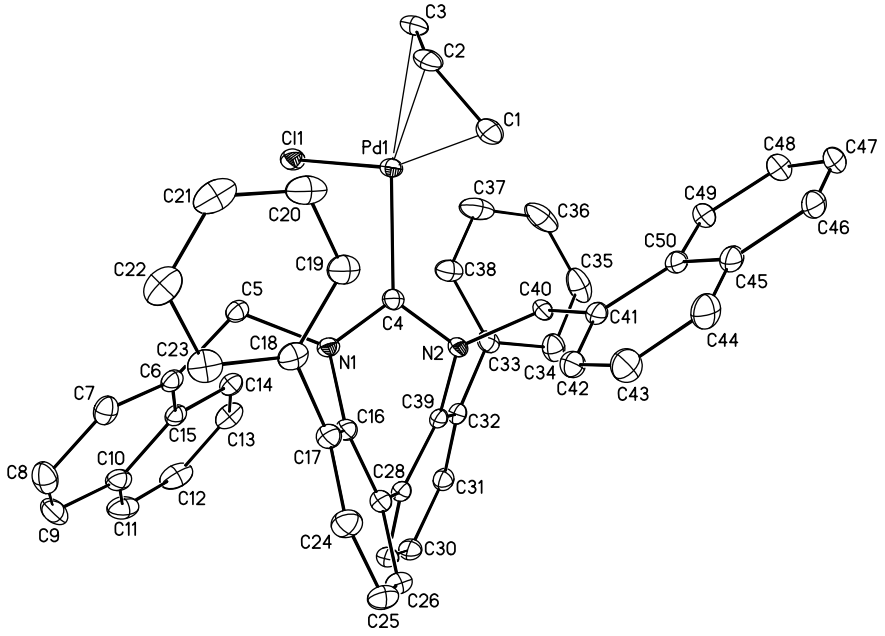
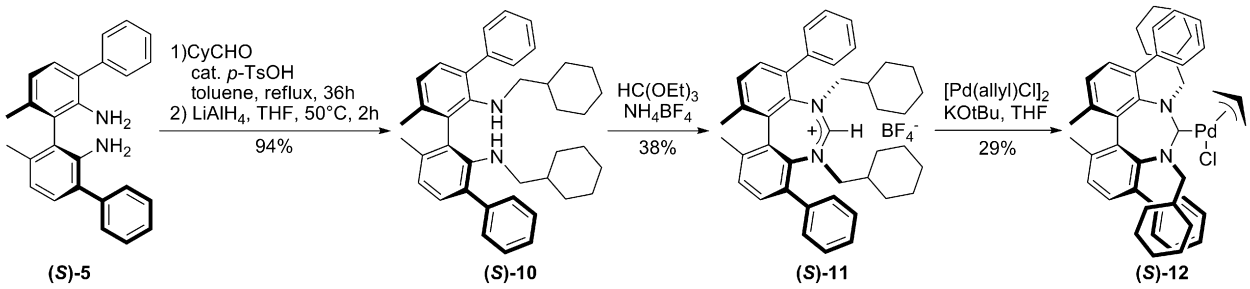
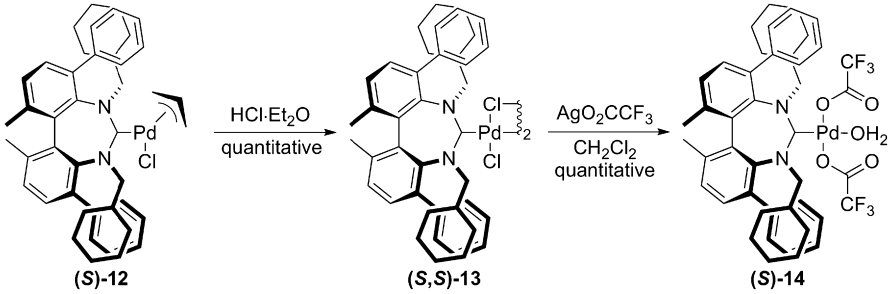


Figure 5. Solid-state molecular structure of **9**. Hydrogen atoms are omitted for clarity. Only the preferred orientation of the disordered atom C2 is shown, which is disordered over two positions in an 85:15 ratio. Thermal ellipsoids are shown at 30% probability.



Scheme 3. Synthesis of the first resolved metal complexes bearing a chiral ^{7}NHC.



Scheme 4. Synthesis of the catalytically relevant resolved ^{7}NHC–Pd complex (***S***)**-14**.

Addition of ethereal HCl to (***S***)**-12** to afford the [NHC-PdCl$_2$]$_2$ complex (***S,S***)**-13** followed by addition of AgO_2CCF_3 (AgTFA) afforded the NHC–Pd(TFA)$_2$(OH$_2$) complex (***S***)**-14** (Scheme 4). The molecular structure of (***S***)**-14** was confirmed in the solid-state by X-ray diffraction analysis (Fig. 6).[23] Unfortunately, the yields of amidinium salt and NHC–Pd(allyl)Cl are quite low, despite extensive attempts to improve them.[26] Nonetheless, these results represented the first successful preparation of resolved ^{7}NHC complexes of this type.

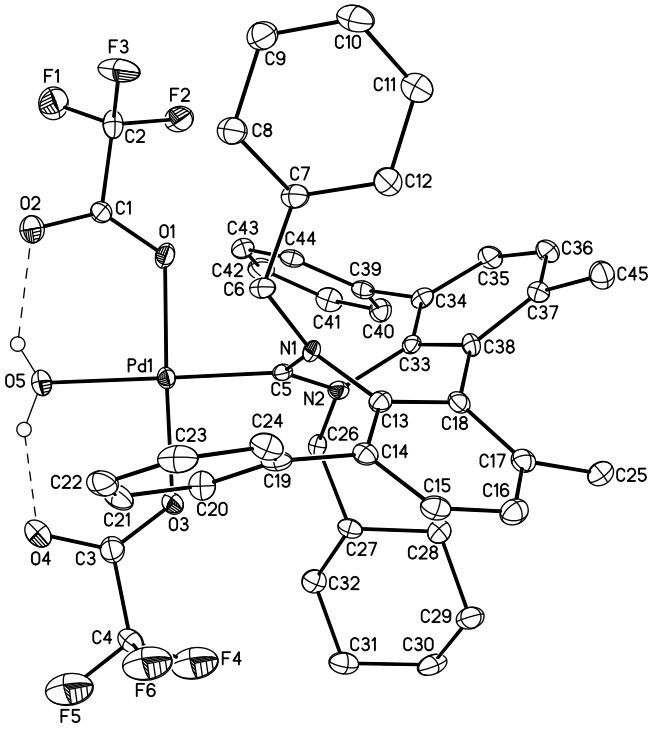
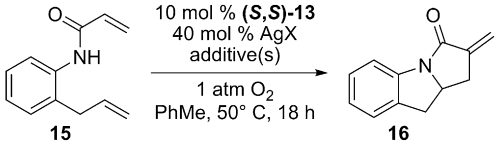


Figure 6. Solid-state molecular structure of (***S***)**-14**. Only one symmetry-independent molecule is shown. All hydrogen atoms except those on the aqua ligand are omitted for clarity. Thermal ellipsoids are shown at 30% probability.

2.3. Initial efforts to apply resolved ^{7}NHC–Pd complexes to asymmetric intramolecular aerobic oxidative amination of alkenes

The [NHC-PdCl$_2$]$_2$ complex (***S,S***)**-13** was first examined as a catalyst for the asymmetric aerobic oxidative cyclization of substrate **15** (Table 1).[27] This substrate was examined because it is the only substrate reported to undergo palladium-catalyzed *asymmetric* aerobic oxidative amination.[28] Yang and co-workers achieved up to 86% ee in the oxidative cyclization of this substrate with a (−)-sparteine-Pd catalyst. NHC ligands have not been tested previously in this oxidative cyclization reaction. Representative screening data in Table 1 reveal only modest success with the use of the ^{7}NHC–Pd complex (***S,S***)**-13** as the catalyst. In the best case, the product **16** was obtained in 63% ee, albeit in rather low yield (Table 1, entry 3). Other conditions examined resulted in significantly lower ee or no formation of **16**. For example, base was shown to facilitate substrate oxidation by Pd^{II}, but ^{i}Pr$_2$NEt was the only base among those tested

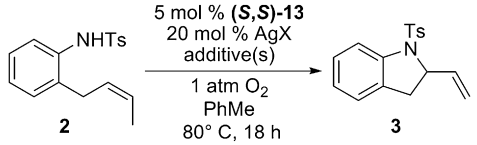
Table 1
Aerobic oxidative cyclization of substrate **15** catalyzed by (***S,S***)**-13**



Entry	AgX	Additive(s)	Yield[a] (%)	%ee[b] (%)
1	AgTFA	^{i}Pr$_2$NEt	24	27
2[c]	AgTFA	^{i}Pr$_2$NEt	25	20
3	AgTFA	^{i}Pr$_2$NEt, 3Å MS	35	63
4	AgOAc	^{i}Pr$_2$NEt	~0	—
5	AgoBz	^{i}Pr$_2$NEt	~0	—
6	AgOTs	^{i}Pr$_2$NEt	~0	—
7	Ag_2CO_3	^{i}Pr$_2$NEt	~0	—

[a] Yield determined by GC relative to internal standard.
[b] % ee determined by GC or HPLC.
[c] Reaction run at 80 °C.

Table 2
Attempts at asymmetric aerobic oxidative cyclization of substrate **2** by **(*S,S*)-13**



Entry	Agx	Additive(s)	Yield[a] (%)	ee[b] (%)
1	AgOAc	—	31	9
2	AgOAc	BzOH[c]	27	−3
3	AgOAc	Na_2CO_3[d]	63	2
4	AgTFA	—	22	1
5	AgTFA	BzOH[c]	20	1
6	AgTFA	Na_2CO_3[d]	26	−7
7	AgTFA	$^iPr_2NEt$,[d] 3Å MS	12	0

[a] Yield determined by GC relative to internal standard.
[b] % ee determined by HPLC.
[c] 20 mol %.
[d] 2 equiv.

(including Na_2CO_3, NaOAc, NaO_2CPh, MgO, $Ca(OH)_2$, NEt_3) that led to even modest levels of catalytic turnover. The origin of these observations is not currently known.

We next turned our attention to the aerobic oxidative amination of substrate **2**, which has been shown by us to be an effective substrate for aerobic oxidative amination catalyzed by NHC–Pd complexes, including one of our racemic [7]NHC ligands (Fig. 2).[14] The conditions employed in entries 1–6 of Table 2 resemble the best conditions for the reported racemic cyclization of **2**,[14] whereas the conditions employed in entry 7 mirrored the best conditions for the cyclization of **15**. Although modest yields of product **3** were obtained, the cyclization product was nearly racemic in every case (Table 2).

2.4. Use of a resolved [5]NHC–Pd complex in asymmetric aerobic oxidative Wacker-type cyclization reactions

When the oxidative cyclization studies described above were nearly complete, Kündig and co-workers reported the use of chiral [5]NHC ligands in Pd-catalyzed intramolecular α-arylation reactions (Fig. 1d).[6,7] The latter work, which provided the first highly-enantioselective reaction (>90% ee) employing a chiral NHC–Pd catalyst, prompted us to examine the most successful [5]NHC ligand from this work in Wacker-type oxidative cyclization reactions.

Synthesis of palladium complexes derived from the amidinium iodide salt **1** (Fig. 1d) were carried out by combining **1** with $[Pd(allyl)Cl]_2$ and KO^{t}Bu to afford the NHC–Pd(allyl)Cl complex **17**, followed by protonolysis of the allyl ligand with ethereal HCl to afford the $[NHC–PdCl_2]_2$ complex **18**.[29] Anion metathesis with silver(I)-carboxylate salts did not furnish the desired NHC–Pd(carboxylate)$_2$ complexes, but instead led to formation of the cyclometalated complexes **19** and **20** (Scheme 5). The solid-state molecular structure of **19**

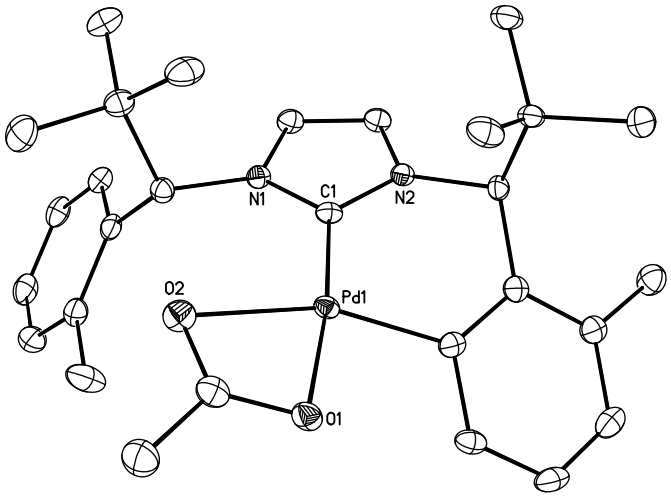
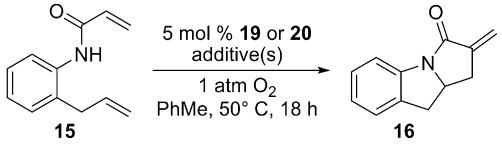


Figure 7. Solid-state molecular structure of **19**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at 50% probability.

was unambiguously determined by X-ray diffraction analysis (Fig. 7).[23] Although complexes **19** and **20** were not the targeted NHC–Pd(carboxylate)$_2$ catalysts, we nonetheless tested these complexes as catalysts for the oxidative cyclization reactions of substrates **2** and **15**.

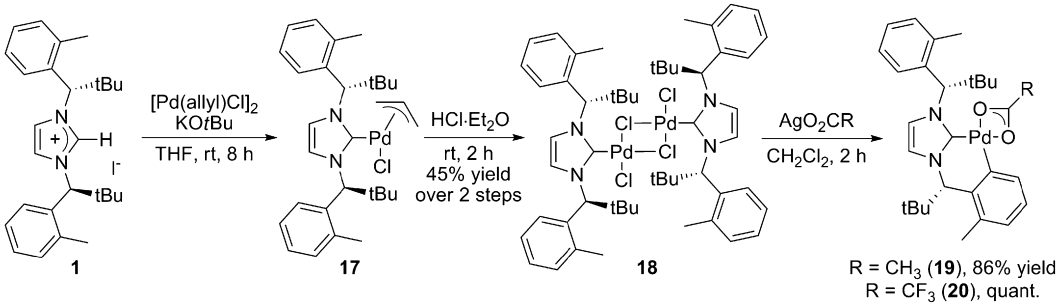
In the aerobic oxidative cyclization of substrate **15** with catalysts **19** and **20**, improved yields could be obtained relative to those with catalyst **(*S,S*)-13**; however, the product **16** was racemic in every case (Table 3). The aerobic oxidative cyclization of **2** with catalysts **19** and **20** proceeded in excellent yield (Table 4), but, once again, the product was always racemic. The improved yields with the

Table 3
Aerobic oxidative cyclization of substrate **15** catalyzed by **19** and **29**



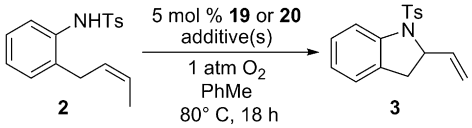
Entry	Catalyst	Additive(s)	Yield[a] (%)	ee[b] (%)
1	**19**	—	57	2
2[c]	**19**	20% BzOH	15	5
3	**19**	2 equiv Na_2CO_3	66	7
4	**19**	2 equiv $^iPr_2NEt$, 3Å MS	34	0
5	**20**	—	5	0
6	**20**	20% BzOH	7	0
7	**20**	2 equiv Na_2CO_3	13	4
8	**20**	2 equiv $^iPr_2NEt$, 3Å MS	2	0

[a] Yield determined by GC relative to internal standard.
[b] % ee determined by HPLC.
[c] Reaction run at 80°C.



Scheme 5. Synthesis of catalytically relevant palladium complexes bearing Kündig's chiral NHC.

Table 4
Aerobic oxidative cyclization of substrate **2** catalyzed by **19** and **20**



Entry	Catalyst	Additive(s)	Yield[a] (%)	ee[b] (%)
1	**19**	—	90%	5%
2	**19**	BzOH[c]	91%	4%
3	**19**	Na_2CO_3[d]	90%	6%
4	**20**	—	82%	5%
5	**20**	BzOH[c]	85%	4%
6	**20**	Na_2CO_3[d]	83%	0%

[a] Yield determined by GC relative to internal standard.
[b] %ee determined by HPLC.
[c] 20 mol %.
[d] 2 equiv.

^{5}NHC–Pd-catalysts may reflect the smaller size of the ^{5}NHC ligand compared to the ^{7}NHC ligand.

3. Conclusions

In this study, we have achieved preparation of the first enantiomerically resolved ^{7}NHC–Pd complexes and investigated their reactivity in aerobic oxidative cyclization reactions of alkenes. The ^{7}NHC-precursor amidinium salt is accessible through a sequence involving a Pd-catalyzed *ortho*-arylation of the biaryl ring, incorporation of nitrogen substituents via reductive amination, and cyclization using $HC(OEt)_3$ and NH_4BF_4 under microwave irradiation. The *ortho*-arylation reaction is critical to access stable ^{7}NHC–Pd complexes. These ligands were employed with mixed success in Pd-catalyzed aerobic oxidative cyclization reactions. In one case, up to 63% ee was achieved in a Pd-catalyzed intramolecular oxidative amination reaction. Although this level of enantioselectivity is relatively modest, the result is significantly better than that obtained with Pd-catalysts bearing a chiral five-membered NHC ligand (≤7% ee). These observations highlight the prospects for the use of chiral seven-membered NHCs of the type described here in asymmetric catalysis.

4. Experimental

4.1. General considerations

Solvents for reactions performed on the benchtop were dried by passing them through a column of activated alumina,[30] whereas solvents for reactions performed in a glove box were dried over Na/benzophenone and distilled. ^{1}H and ^{13}C NMR spectra were recorded on 300 or 500 MHz spectrometers. ^{1}H chemical shifts (δ) are reported in parts per million relative to $SiMe_4$ (0.0 ppm) while ^{13}C chemical shifts are reported in parts per million relative to deuterated solvent (77.23 ppm for $CDCl_3$ or 128.06 for benzene-d_6).

4.2. General screening conditions for oxidative Wacker-type cyclization reactions

Screening was conducted in disposable Borosilicate Heavy Wall 13×100 mm Culture Tubes (Fisherbrand). Catalyst and solid additives were weighed into reaction tubes, which were then loaded onto a custom 48-well parallel reactor mounted on a Large Capacity Mixer (Glas-Col). The headspace was purged under a positive flow of dioxygen with mild vortexing for 15 min. A stock solution of the substrate in toluene (0.1 M) was added to the reaction tubes, which were then vortexed for 18 h under 1 atm dioxygen at 80 °C, after which time the reactions were filtered over Celite and the solvent was removed from each tube under reduced pressure prior to analysis by ^{1}H NMR spectroscopy, gas chromatography, and/or HPLC.

4.3. Synthesis and characterization data

*4.3.1. N,N′-Bis(1-naphthylmethyl)-2′,2″-diamino-m,m-quaterphenyl (**7**)*

Diamine **6** (470 mg) was combined with 778 μL 1-naphthaldehyde and a few crystals of *p*-TsOH in ~250 mL toluene. A Dean–Stark apparatus was attached, and the reaction was heated to reflux for 48 h. Solvent was then removed in vacuo and the residue was taken up in 25 mL dry THF. 339 mg $LiAlH_4$ (6.4 equiv) was added slowly and the solution was heated to 50 °C for 2 h. After cooling to room temperature, the reaction was carefully quenched by sequential addition of 0.3 mL H_2O, 0.6 mL 10% $NaOH_{(aq)}$, then 0.9 mL H_2O. The solid that formed was removed by filtration, and the filtrate was concentrated in vacuo. Product was purified by column chromatography (SiO_2 packed with 5% NEt_3 in toluene, then flushed with toluene before loading crude) using a gradient eluent (pure toluene to 1:1 toluene–EtOAc) to afford 605 mg **7** as a light yellow oil (70% yield). HRMS: *m*/*z* (ESI) calculated $[MH]^+$=617.2956, measured 617.2963 (Δ=1.1 ppm). ^{1}H NMR (300 MHz, $CDCl_3$) 3.99 (s, 4H) 6.90 (d, *J*=6.0 Hz, 2H), 7.01 (t, 7.5 Hz, 2H), 7.14–7.36 (m, 22H), 7.60 (d, *J*=8.4 Hz, 2H), 7.69 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 50.6, 121.8, 123.6, 125.4, 125.6, 126.3, 127.2, 127.9, 128.5, 128.5, 129.4, 130.9, 131.1, 132.5, 133.8, 134.2, 135.6, 140.9, 145.0.

*4.3.2. Amidinium salt **8***

Diamine **7** (3.1 g) was combined with 560 mg NH_4BF_4 in 150 mL $HC(OEt)_3$. The reaction was heated to 130 °C for 48 h. The reaction was then concentrated in vacuo to a thick oil and taken up in minimal methylene chloride. Excess hexanes were added to drive the product out of solution, and the suspension was cooled in a freezer overnight. Tan solid was collected by filtration and washed with pentane. The solid was then taken up in minimal refluxing ethanol and cooled in a freezer. The resultant powder was collected by filtration, washed with pentane, and dried under high vacuum to afford 1.7 g pure **8** as a tan solid (47% yield). HRMS: *m*/*z* (ESI) calculated $[MH]^+$=627.2795, measured 627.2805 (Δ=1.6 ppm). ^{1}H NMR (300 MHz, $CDCl_3$) 4.35 (d, *J*=14.4 Hz, 2H), 4.82 (d, *J*=14.4 Hz, 2H), 6.73 (br s, 4H), 7.04 (ddd, *J*=8.1, 6.9, 1.2 Hz, 2H), 7.10–7.15 (m, 4H), 7.21 (ddd, *J*=8.4, 6.9,1.2 Hz, 2H), 7.28–7.31 (m, 4H), 7.36–7.54 (m, 10H), 7.61 (d, *J*=7.8 Hz, 2H), 7.68 (d, *J*=8.4 Hz), 9.49 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) 57.1, 122.2, 125.9, 126.0, 126.7, 128.0, 128.9, 129.1, 129.3, 129.6, 130.1, 130.2, 132.2, 132.4, 133.8, 134.3, 136.9, 137.2, 142.1, 179.1.

*4.3.3. NHC–Pd(allyl)Cl complex **9***

Compound **8** (756 mg, 1.06 mmol), KO^{t}Bu (132.2 mg, 1.1 equiv), and $[Pd(allyl)Cl]_2$ (230 mg, 0.60 equiv) were combined in 30 mL dry THF in a glove box. The reaction was stirred at room temperature for 20 h, after which it was removed from the glove box. The suspension was filtered over Celite and the solvent removed in vacuo. Compound **9** was purified by column chromatography (SiO_2) using a gradient eluent (40% Et_2O in hexanes to pure Et_2O) as a lightly yellow solid (100 mg, 12% yield). The product is a 1.5:1 mixture of allyl rotamers by ^{1}H NMR spectroscopy. HRMS: *m*/*z* (ESI) calculated $[M(-Cl)]^+$=771.2169, measured 771.2178 (Δ=1.2 ppm). ^{1}H NMR (300 MHz, CDCl3) (all peaks are quite broad. Identity is known from X-ray crystal structure, but NMR spectra are difficult to interpret) 1.64 (m, 1.5H), 2.25 (m, 1H), 2.38 (m, 1H), 2.84 (m, 1.5H), 3.31 (m, 2.5H), 4.29 (m, 1.5H), 4.72 (m, 1H), 5.00 (m, 1.5H), 5.24 (m, 1H), 6.94–7.64 (m, 45H). ^{13}C NMR (75 MHz, $CDCl_3$) 58.2 (br peak), 115.7, 116.4, 125.0, 125.7, 127.7, 127.9, 128.4, 129.1, 132.0, 133.4, 136.2, 140.1, 144.9 (br peak).

4.3.4. (S)-N,N′-Bis(cyclohexylmethyl)-2′,2″-diamino-4′,4″-dimethyl-m,m-quaterphenyl ((**S**)-**10**)

Diamine **(*S*)-5** (2.0 g) was combined with 1.7 mL cyclohexane carboxaldehyde (2.5 equiv) and a few crystals of *p*-TsOH in 120 mL toluene in a Dean–Stark apparatus. The reaction was heated to reflux for 60 h, cooled to room temperature, and solvent was removed in vacuo. The resultant residue was taken up in 50 mL dry THF and 650 mg $LiAlH_4$ was carefully added portionwise. The reaction was stirred at 50 °C for 2 h, cooled to room temperature, and carefully quenched by sequential addition of 1 mL H_2O, 2 mL 10% $NaOH_{(aq)}$, and 3 mL H_2O. The solid, which had crashed out was removed by filtration, and solvent was removed from the filtrate in vacuo to afford **(*S*)-10** in 95% yield. HRMS: *m*/*z* (ESI) calculated $[MH]^+$=557.3891, measured 557.3883 (Δ=1 ppm). ^1H NMR (300 MHz, CDCl3) 0.41 (br q, *J*=12.3 Hz, 4H), 0.90–1.09 (m, 8H), 1.20–1.28 (m, 4H), 1.48–1.55 (m, 4H), 2.02 (s, 6H), 2.27 (m, 4H), 3.27 (br s, 2H), 6.87 (dd, *J*=7.8, 0.8 Hz, 2H), 7.10 (d, *J*=7.6 Hz, 2H), 7.27–7.30 (m, 2H), 7.35–7.40 (m, 4H), 7.49–7.52 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) 20.5, 26.1, 26.7, 30.9, 31.0, 38.8, 54.5, 121.9, 126.5, 127.6, 128.4, 129.1, 131.3, 137.1, 142.4, 145.8.

4.3.5. Amidinium salt (**S**)-**11**

Diamine **(*S*)-10**, NH_4BF_4 (1.3 equiv), and 100 mL $HC(OEt)_3$ were combined and subjected to microwave irradiation (equilibration time to 100 °C=10 min, 2 h at 100 °C, max power=250 watts). Concentration on a rotary evaporator, dissolving in minimal hot toluene, and crashing out with hexanes afforded some powder and a sticky orange semi-solid. The powder was filtered away, and the semi-solid was again taken up in hot toluene and crashed out with hexanes. This procedure was repeated as necessary until no more powder formed. Dissolved filtered powder in dichloromethane and filtered to remove excess NH_4BF_4. Removed solvent from filtrate to afford a sticky solid, which was re-dissolved in minimal dichloromethane and added dropwise to a 250 mL graduated cylinder filled with hexanes (powder forms immediately on addition of each drop). After complete addition, let suspension sit for 30 min then decanted the hexanes. Dissolved solid in dichloromethane and transferred to a flask. Solvent was removed in vacuo to afford 38% yield (1.35 g) of **(*S*)-11** as a tan powder. HRMS: *m*/*z* (ESI) calculated $[MH]^+$=567.3734, measured 567.3736 (Δ=0.4 ppm). ^1H NMR (300 MHz, CDCl3) 0.39 (qd, *J*=11.7 Hz, 2H), 0.52–0.71 (m, 4H), 0.81–0.97 (m, 4H), 1.10–1.35 (m, 6H), 1.39–1.43 (m, 6H), 2.29 (s, 6H), 2.93 (dd, *J*=13.8, 5.1 Hz, 2H), 3.37 (14.0, 6.1 Hz, 2H), 7.27–7.35 (m, 6H), 742–7.49 (m, 4H), 7.55–7.61 (m, 4H), 9.05 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) 19.6, 25.6, 25.7, 25.8, 29.7, 30.0, 40.1, 61.4, 127.7, 128.9, 130.1, 131.0, 132.6, 132.8, 134.4, 137.6, 138.3, 145.4, 175.8.

4.3.6. NHC–Pd(allyl)Cl complex (**S**)-**12**

This complex was synthesized analogously to compound **9**. Product was purified by column chromatography (SiO_2) using 1:1 Et_2O–hexanes as the eluent. Product was isolated in 29% yield (195 mg) as a lightly yellow solid. Peaks in NMR spectra are challenging to assign, and this structure is assigned from previous precedent,[15] ^1H NMR spectroscopy (dr ~2.2:1), and from reactivity ((**S**)-**14** is derived quantitatively from this species, which has been fully characterized using ESI-MS, ^1H and ^{13}C NMR spectroscopy, and single-crystal X-ray diffraction analysis). ^1H NMR (300 MHz, CDCl3) 0.47–1.40 (m, 31.9H), 2.15–2.53 (m, 10.15H), 2.53–3.05 (m, 4.8H), 3.34–3.65 (m, 4.25H), 4.33 (m, 2H), 5.23 (m, 0.45H), 5.39 (m, 1H), 7.09–7.37 (m, 20.3H).

4.3.7. $[NHC\text{-}PdCl_2]_2$ complex (**S,S**)-**13**

Compound **(*S*)-12** (195 mg, 0.26 mmol) was dissolved in 50 mL Et_2O, and 3.25 mL 2.0 M ethereal HCl (25 equiv) was added via syringe. This mixture was stirred at room temperature for 6 h, over which time the solution turned bright yellow. Removed solvent in vacuo and dried under high vacuum to afford 195 mg of a bright yellow compound, which reacts as the drawn compound when combined with AgO_2CCF_3 (below). ^1H NMR spectroscopy revealed two large broad peaks, in the alkyl and aryl regions, but no distinct peaks were observed. Peaks in NMR spectra are challenging to assign, and this structure is assigned from previous precedent,[15] and from reactivity ((**S**)-**14** is derived quantitatively from this species, which has been fully characterized using ESI-MS, ^1H and ^{13}C NMR spectroscopy, and single-crystal X-ray diffraction analysis).

4.3.8. NHC–$Pd(O_2CCF_3)_2(OH_2)$ complex (**S**)-**14**

Compound **(*S,S*)-13** (83 mg, 0.056 mmol) was combined with 54.2 mg (4.4 equiv) AgO_2CCF_3 in dichloromethane. This reaction mixture was stirred at room temperature for 1.5 h, during which time a white solid was observed to have formed. Filtration over Celite and removal of solvent under vacuum afforded **(*S*)-14** as a tan-yellow solid in quantitative yield. The identity of this species was confirmed by X-ray crystallographic analysis (Fig. 6). ESI-MS: *m*/*z* (major peak containing Pd) 707.7 ($[NHC\text{-}Pd(OH_2)(OH)]^+$). ^1H NMR (300 MHz, CDCl3) 0.39–0.51 (m, 4H), 0.83–1.44 (m, 18H), 2.19 (s, 6H), 3.23 (dd, *J*=13.5, 5.1 Hz, 2H), 4.32 (dd, *J*=13.2, 8.1 Hz, 2H), 7.18 (d, *J*=7.5 Hz, 2H), 7.31 (d, *J*=7.5 Hz, 2H), 7.46–7.52 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) 19.6, 25.5, 25.9, 26.1, 29.8, 30.8, 38.4, 60.3, 128.5, 128.6, 129.4, 129.7, 132.0, 133.3, 134.3, 137.6, 139.4, 145.1, 201.8. $[\alpha]_D^{25}$ +3.6 (*c* 5.5, CH_2Cl_2).

4.3.9. NHC–Pd(allyl)Cl complex **17**

In a glove box, amidinium salt **1** (285 mg, 0.552 mmol), $[Pd(allyl)Cl]_2$ (131 mg, 0.65 equiv), and KO*t*Bu (80 mg, 1.3 equiv) were combined in 20 mL THF. The reaction stirred at room temperature in the dark for 12 h, after which time the reaction flask was removed from the glove box and exposed to ambient conditions. Solvent was removed on a rotary evaporator, and product was isolated by column chromatography (SiO_2) using 1:1 Et_2O–hexanes as the eluent to afford a light tan solid with a ^1H NMR spectrum, which could be consistent with the drawn product, but was not conclusive. Carried material forward without full characterization. Identity is based on formation of **19** and **20**.

4.3.10. $[NHC\text{-}PdCl_2]_2$ complex **18**

To crude **17** was added 1 mL ethereal HCl (2.0 M, 3.6 equiv compared to amidinium salt **1**). The reaction was stirred at room temperature for 2 h. Solvent was removed on a rotary evaporator to afford 141 mg **18** as an orange–brown solid in 45% yield over two steps. Again, the ^1H NMR spectra were consistent with the drawn product, but inconclusive. Assignment is based on formation of **19** and **20**. ^1H NMR (300 MHz, CDCl3) (all peaks are broad) 1.06–1.16 (m, 36H), 3.29 (s, 6H), 3.34 (s, 6H), 6.92 (s, 2H), 7.07–7.23 (m, 12H), 7.38 (s, 2H), 7.66 (s, 4H).

4.3.11. Pd complex **19**

Compound **18** (81 mg, 0.072 mmol) was combined with 49 mg AgOAc (4.1 equiv) in dichloromethane. The reaction stirred at room temperature in the dark for 2 h, after which time the reaction was filtered through Celite to remove the AgCl. Solvent was removed in vacuo to afford 74 mg **6** (86% yield) as a brown solid. The structure of **19** was unambiguously assigned by X-ray diffraction analysis (Fig. 4): X-ray-quality crystals were obtained from slow evaporation of a $CDCl_3$-solution of **6** in a round-bottom flask. An X-ray-quality crystal of **6** was re-dissolved in $CDCl_3$, and gave a ^1H NMR spectrum, which was identical to the bulk material. HRMS: *m*/*z* (ESI) calculated $[M–OAc]^+$=491.1836, measured 491.1830 (Δ=1.0 ppm). ^1H NMR (300 MHz, CDCl3) 1.09 (s, 9H), 1.26 (s, 9H), 2.11 (br s, 6H), 2.32 (s, 3H), 2.94 (s, 3H), 5.13 (s, 1H), 6.26 (s, 1H), 6.79–6.99 (m, 2H), 6.99 (d, *J*=2.1 Hz, 1H), 7.10–7.16 (m, 4H), 7.37–7.48 (m, 2H), 7.49 (dd, *J*=5.4, 4.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) 21.8, 22.1, 27.4, 29.3, 37.3, 37.7, 66.1, 71.8, 118.0, 123.0, 125.5, 126.1, 127.2, 127.8, 128.2, 131.4, 131.5, 134.0, 135.7, 136.4, 138.9, 139.2, 162.2, 174.2.

*4.3.12. Pd complex **20***

Prepared from **18** analogously to the above synthesis of **19**, using AgO_2CCF_3 in place of AgOAc. Product was obtained in ~100% yield (67 mg) as a dark brown solid. HRMS: *m*/*z* (ESI) calculated $[M]^+$=491.3426, measured 491.3437 (Δ=2.2 ppm). ^{1}H NMR (300 MHz, CDCl3) (all peaks are rather broad) 1.03–1.29 (m, 36H), 2.33 (m, 6H), 2.51 (m, 6H), 5.84–5.92 (m, 4H), 7.03–7.91 (m, 16H), 8.89 (br s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 15.5, 21.4, 21.7, 27.1, 27.4, 27.6, 28.2, 38.3, 39.4, 66.1, 66.9, 72.4, 118.7, 123.1, 124.7, 125.0, 127.3, 128.4, 129.3, 129.6, 132.0, 133.2, 134.1, 137.0, 137.3, 146.7, 147.4.

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