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NCN–pincer palladium complexes with multiple anchoring points for functional groups

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Dedicated to Dr. Jaap Boersma on the occasion of his 65th birthday.

Contents

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Abstract

para-Substituted NCN–pincer palladium(II) complexes (NCN = [2,6-$(CH_2NMe_2)_2C_6H_3]^-$) of the type $[Pd(OH_2)$(NCN-4-CHZ-$C_6H_4SiMe_3)](BF_4)$ (with Z = OH, OAc, $OSiMe_2$t-Bu, $(C_5H_5N)(BF_4)$) have been synthesized and were used as catalysts in the aldol reaction between methyl isocyanoacetate and *para*-functionalized benzaldehydes. The applied substituents Z, placed on a distal position from the cationic palladium(II) site, do not significantly influence the catalytic activity and selectivity of the resulting complexes, but offer a useful starting point for further modification or functionalization.

Keywords: Palladium; Ligand design; Synthesis; Catalysis

1. Introduction

The use of functionalized ligands in organometallic and coordination chemistry is a common tool to immobilize a complex, alter its solubility, or tune the metal center electronically. Our interest is focused on the *para*-functionalization of NCN–pincer metal complexes (NCN = 2,6-bis[(dimethylamino)methyl]phenyl anion) [1–5] with a wide variety of different substituents and anchoring points. Variation of the *para*-substituent Z in NCN–Z metal complexes can be exploited to fine-tune the electronic, catalytic, spectroscopic, and diagnostic properties of the complexes and can furthermore be used to advantage in a synthetic sense for the further modification of pincer complexes. In this regard, we have extensively studied NCN–pincer metal complexes of the nickel triad (Ni, Pd, Pt). NCN–Z nickel(II) complexes, e.g., show a remarkable relation between the Ni(II)/Ni(III) oxidation potential and the electronic nature of *para*-substituent Z [3]. A linear Hammett relationship was established between the σ_p-Hammett substituent constant and the oxidation potential, which translated itself consequently to the overall catalytic reactivity of the complexes in the redox-based Karasch-addition of CCl_4 to methyl metacrylate. Later, we observed similar linear relationships in NCN–Z platinum(II) complexes between the *para*-substituent Z and both the ^{195}Pt NMR chemical shift and the calculated Mulliken populations (DFT) on platinum [6]. These observations very nicely show the electronic and catalytic fine-tuning capabilities of the *para*-substituents in these pincer complexes, as well as the predictive power of their effects on the metal center.

For further modifications on NCN–Z metal complexes the Pd and Pt complexes are especially suitable, since they are highly stable, even allowing functionalization after metalation of the ligand [6–8]. This makes them excellent building blocks for the construction of new (catalytic) organometallic materials [1,9]. *Para*-hydroxy [10,11] and *para*-alkynyl NCN–pincer platinum halide complexes [12] form non-covalent linear organometallic main chain polymers. The direct lithiation of *para*-halo NCN–pincer platinum complexes at −100 °C allows access to *para*-lithio complexes [6–8] which can be further reacted with appropriate electrophiles or lead to the formation of covalent organometallic main-chain polymers. A remarkable ‘organic transformation’ that exemplifies the chemical stability of both NCN–pincer palladium and platinum complexes is the direct sulfonation of the *para*-position of the non-substituted complexes by treatment with $HOSO_2Cl$ at room temperature to yield the corresponding *para*-sulfato complexes in 18 and 25% isolated yield, respectively [6,7].

Especially successful has been the immobilization of NCN–pincer complexes on a variety of molecular support systems for diagnosis applications and for catalyst recycling purposes. Using *para*-functionalities, NCN–pincer platinum complexes were attached to bio-scaffolds like carbohydrates [13] and peptides [14,15]. Because of the reversible binding properties of the NCN–pincer platinum complexes with SO_2 and I_2 [1,16], and the concomitant reversible color change from colorless to orange and purple, respectively, these conjugates are interesting candidates as biomarkers and biosensors. We have extensively investigated the immobilization of NCN–pincer complexes onto soluble and molecular supports for catalyst recycling, for which supports as structurally diverse as benzene rings [17–19], dendrons [20], dendrimers [21–27], hyperbranched polymers [28–31], and dendronized polymers [32] were used to covalently, as well as non-covalently immobilize these complexes. One of the major applications for which the resulting hybrid materials are tested is their use in nano-filtration set-ups for the continuous as well as batch-wise operation and separation of homogeneous catalysts [33].

Here, we report the synthesis of catalytically active cationic NCN–pincer palladium(II) complexes **1**–**4** functionalized with two anchoring points, thus allowing both immobilization and the introduction of additional functional groups, e.g., hydroxyl, acetyl, and pyridinium, in the vicinity of the metal complex (Plate 1). These cationic complexes were tested as catalysts in C–C coupling reactions between methyl isocyanoacetate and (functionalized) benzaldehydes.

Complexes **1**–**4** are all substituted with a trimethylsilyl group. This trimethylsilyl group is used as a mimic for carbosilane dendritic support systems. Earlier results indicated that once attachment to trimethylsilyl chloride is feasible, the method also holds for attachment to dimethylchlorosilyl functionalized carbosilane dendrons [23,24,26,28].

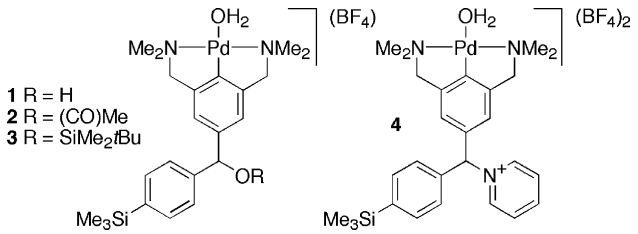


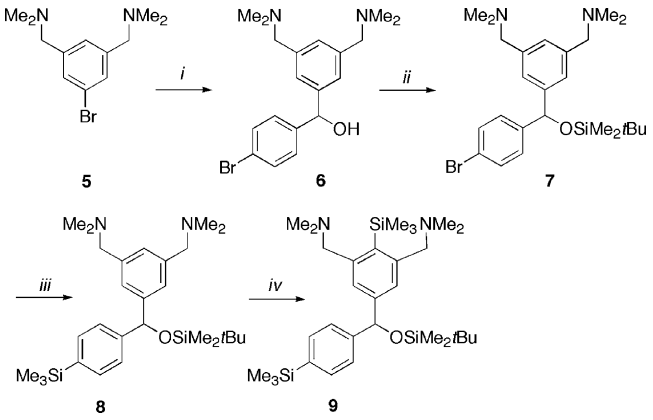
Plate 1. Hydroxyl (**1**), acetyl (**2**), siloxy (**3**), and pyridinium (**4**) functionalized NCN–pincer palladium(II) complexes.

2. Results

2.1. Synthesis

Complexes **1**–**4** were synthesized from a single ligand precursor (**9**), which was obtained according to the route depicted in Scheme 1. Lithiation of 1-bromo-3,5-bis-[(dimethylamino)methyl]benzene (**5**) with two equivalents of *t*-BuLi, followed by a quench with 4-bromobenzaldehyde, afforded the *para*-substituted ligand **6**. Protection of the benzylic alcohol with a *t*-butyldimethylsilyl group (TBDMS) proceeded quantitatively in THF. The resulting silyl ether **7** was reacted with two equivalents of *t*-BuLi and subsequently quenched with trimethylsilyl chloride. This reaction afforded compound **8** in good yield. A second trimethylsilyl substituent was introduced on the position *ortho* with respect to both nitrogen donor atom-containing substituents, by selective deprotonation with *n*-BuLi in hexanes, and subsequent treatment with Me_3SiOTf (OTf = trifluoromethylsulfonate) in THF, affording **9** as a single product in an overall yield of 67% based on **5**.

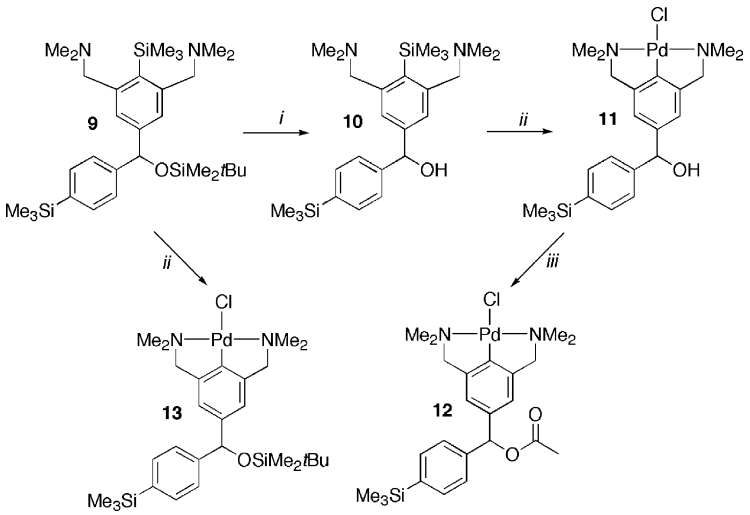
Complexes **11**, **12** and **13** were obtained from **9**, as depicted in Scheme 2. Deprotection of the benzylic alcohol function of **9** with NBu_4F in THF to obtain ligand **10** proceeded smoothly and in high yield (94%). Palladation of **10**



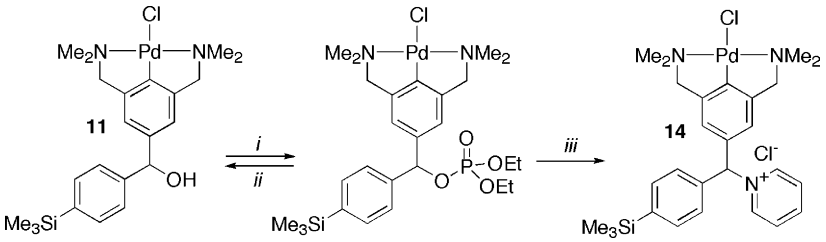
Scheme 1. Synthesis of ligand **9**: (i) 2 *t*-BuLi, 4-bromobenzaldehyde, NH_4Cl; (ii) $SiMe_2t$-BuCl, imidazole; (iii) 2 *t*-BuLi, $SiMe_3Cl$; (iv) *n*-BuLi, $SiMe_3OTf$.

with $Pd(OAc)_2$ in methanol followed by treatment with LiCl afforded complex **11**, containing a hydroxyl group, in a satisfactory 89% yield. The high stability of the NCN–pincer palladium complex [6–8] enabled us to react the benzylic hydroxyl group with acetic anhydride in the presence of pyridine to obtain the acetyl functionalized complex **12** in a 87% yield, without observable decomposition of the organometallic moiety. Direct palladation of **9** in a similar manner as for **10** afforded complex **13** as the only product, isolated in 92% yield.

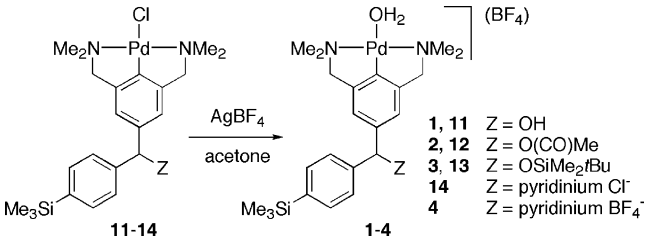
Attempts were made to functionalize the benzylic alcohol moiety of palladium complex **11** with a diethylphosphate moiety. Reaction of complex **11** with chloro diethylphosphate in the prescence of various bases, i.e. triethylamine or diisopropylethylamine, yielded the desired diethylphosphate. Attempted isolation of the product by aqueous work-up led to the quantitative removal of the phosphate giving back alcohol **11**. The use of pyridine as solvent and internal base in the esterification of **11** with chloro diethylphosphate, unintendedly



Scheme 2. Synthesis of palladium complexes **11**–**14**: (i) NBu_4F; (ii) (a) $Pd(OAc)_2$, (b) LiCl; (iii) Ac_2O/pyridine.



Scheme 3. Reversible formation of the diethylphosphate substituted NCN–palladium complex, and formation of **14**: (i) $ClPO(OEt)_2$, base; (ii) H_2O; (iii) pyridine.



Scheme 4. Dehalogenation of **11**–**14** to obtain the catalytically active cationic palladium-aqua complexes **1**–**4**.

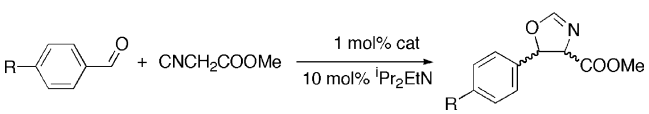
led to pyridinium complex **14** as the sole product in 85% isolated yield (Scheme 3).

2.2. Catalytic activity in aldol condensations

Complexes **11**–**14** were converted into their corresponding cationic aqua complexes by treatment with $AgBF_4$, resulting in the formation of complexes **1**–**4**, respectively (Scheme 4). The additional chloride present in pyridinium complex **14** was removed by adding an additional equivalent of $AgBF_4$ to obtain the dicationic complex **4** as the bis-tetrafluoroborate salt.

Cationic NCN–pincer palladium(II) aqua complexes can serve as catalyst in Lewis acid catalyzed aldol type reactions, such as the addition of methyl isocyanoacetate to benzaldehydes, to produce a diastereomeric mixture of oxazolines (Scheme 5) [34–38].

The catalytic activity of cationic complexes **1**–**4** was tested in this aldol reaction, applying initially dichloromethane as the commonly used solvent [39–47]. However, the low solubility of 4-hydroxymethyl- and 4-hydroxybenzaldehyde in this solvent led to extremely slow conversions. Hence, these reactions were carried out in THF to solubilize the substrate. The results from the experiments are collected in Table 1.



Scheme 5. Aldol condensation catalyzed by NCN–palladium complexes between methyl isocyanoacetate and *para*-substituted benzaldehydes; R = H, CH_2OH, OH.

Table 1
Results from the aldol reaction of methyl isocyanoacetate and (para-substituted) benzaldehyde catalyzed by complexes **1**–**4**[a]

Complex	k (10^{-3} h^{-1})[b]	Conversion (%, after 24 h)
Benzaldehyde (R = H)		
1 (Z = OH)	314	93
2 (Z =OAc)	259	95
3 (Z = OTBDMS)	340	93
4 (Z = Pyridinium)	132	80
4-Hydroxymethylbenzaldehyde (R = CH_2OH)[c]		
1	108	80
2	102	77
3	114	81
4	192	99
4-Hydroxybenzaldehyde (R = OH)[c]		
1	90	58
2	78	55
3	90	60
4	118	72

[a] Conditions: see experimental section.
[b] Initial rate of methyl isocyanoacetate consumption, determined for conversions <40%.
[c] In THF.

The product distributions of the formed oxazolines were similar for all catalysts. The use of benzaldehyde and 4-hydroxybenzaldehyde as substrates led to the formation of oxazolines with *cis*/*trans* ratios amounting to 60/40 and 70/30, respectively. The *cis*/*trans* ratios were not determined for the products obtained from 4-hydroxybenzaldehyde, due to the gradual build up of various side-products upon prolonged reaction times.

3. Discussion

3.1. Synthesis

The selective and quantitative introduction of a trimethylsilyl substituent by a lithiation-transmetallation procedure to produce intermediate **8**, opens the way to immobilize the para-substituted NCN-moiety on carbosilane dendrimers for catalyst recovery and recycling purposes. An important factor in dendrimer synthesis is the necessity to have high conversions and selectivities for all reactions performed on dendrimers, to prevent the formation of extensive defects in the products. Thus, reactions performed on **8** and products

obtained from it should be selective and quantitative. Indeed, the introduction of a trimethylsilyl substituent to C_{ipso} (**9**), the deprotection of the alcohol (**10**), the palladation (**11**), and all subsequent transformations proceeded quantitatively, although loss of material during work-up procedures can lead in certain cases to reduced isolated yields.

The above-mentioned observations strongly indicate that the performed transformations can be used to selectively synthesize dendritic analogues of complexes **1**–**4**. Interesting to note is that the used two-step palladation route, involving lithiation and silylation of C_{ipso} and subsequent electrophilic aromatic palladation [48], is preferred over a direct lithiation-transpalladation route [49]. The latter does not lead to quantitative palladation of the NCN–pincer ligand. An additional advantage of the first route is the inertness of the trimethylsilyl group towards a wide variety of reaction conditions, allowing various modifications on the ligand prior to palladation. Functionalization of benzylic hydroxyl NCN–pincer palladium(II) complex **11** with a diethylphosphate group results in a material that is unstable towards (weak) nucleophiles such as water. This reactivity is incompatible with the presence of nucleophiles in the envisaged catalytic experiments (aldol reactions), making the diethyl phosphate functionalized complex an unsuitable catalyst, but offers a suitable starting material for further functionalizations. Finally, it is noteworthy that the routes to complexes **12** and **14** involve organic functionalization steps on the ligand of the organometallic complex itself.

3.2. Catalytic activity in aldol condensations

Of interest in the study of the catalytic properties of complexes **1**, **2** and **4**, is the influence of the hydroxyl, acetyl, or pyridinium substituents on catalysis. These substituents are, in principle, capable of hydrogen bonding or attractive Coulombic interactions with selected substrates [50]. These interactions can be excluded for silyl functionalized complex **3**, which is therefore used as reference catalyst. Interesting to note for the application of **1**–**4** in catalysis is that a chiral center is formed on the *para*-position of the NCN–pincer ligand during the first step of their synthesis. However, no attempts were made to separate and isolate the compounds in their enantiomerically pure form.

Complexes **1**–**3** have similar activities and product distributions in the aldol reaction with benzaldehyde, 4-hydroxymethylbenzaldehyde, and 4-hydroxybenzaldehyde. Pyridinium functionalized complex **4** is significantly less active in the aldol reaction with benzaldehyde, whereas in the reaction with 4-hydroxymethylbenzene a two-fold increase in activity is found. Low activities are observed for all catalysts in aldol reactions with 4-hydroxybenzaldehyde, albeit that **4** has a somewhat enhanced activity. This increased activity of **4** in the aldol reactions with hydroxyl-functionalized benzaldehydes, indicates a positive effect of the cationic pyridinium site on the catalytic performance of the NCN–palladium complex. One might speculate on the origin of this enhanced catalytic activity for the hydroxyl functionalized substrates. Hydrogen bonding interactions between the co-catalyst ($^{i}Pr_2EtN$) and the hydroxyl function, leading to a build-up of negative charge on the oxygen atom, could result in an attractive interaction with the pyridinium cation of **4**. This interaction brings the aldehyde substrate in the vicinity of the catalytic site, possibly resulting in enhanced reaction rates [51]. Such an interaction between the amine and the alcohol, which is more pronounced for the more acidic phenolic alcohol, could also account for the low rates and conversions observed for 4-hydroxybenzaldehyde. Protonation of large amounts of the base by the acidic phenolic hydrogen inhibits its activity as cocatalyst [52]. No effect of the hydroxyl and acetyl substituents of **1** and **2** was observed on their catalytic activity. Apparently, the capability of the alcohol or ester moiety to participate in hydrogen bond formation with the substrate does not affect the catalytic performance of these complexes.

4. Conclusions

The construction of multi-functionalized NCN–pincer complexes **1**–**4**, illustrates the potential of the NCN–pincer moiety in the construction of new organometallic materials. Extension of the presented synthetic methodologies would allow the introduction of a variety of functional groups to tune and optimize the catalytic behavior of the resulting complexes. These functional groups can act as cocatalyst (a sterically hindered amine base), as supramolecular receptor sites for substrate molecules, or as steric bulk to encapsulate the catalyst. The additional possibility to immobilize the presented systems on (dendritic) supports can be advantageous for recycling purposes.

5. Experimental section

5.1. General

All experiments using air and water sensitive reagents were conducted in a dry nitrogen atmosphere using standard Schlenk techniques. Solvents were dried over appropriate agents and distilled prior to use. The reagent 1-bromo-3,5-bis((dimethylamino)methyl)benzene (**5**) was prepared according to previously reported procedures [53]. Elemental analyses were performed by H. Kolbe, Mikroanalytisches Laboratorium, Mülheim, Germany. ^{1}H and ^{13}C NMR spectra were recorded at 298 K on a Varian Inova 300 or Mercury 200 spectrometer.

5.2. Synthesis

5.2.1. 4-[2,6-$(NMe_2CH_2)_2C_6H_3$-4-CH(OH)]C_6H_4Br (6)

To a precooled (−90 °C) solution of **5** (4.11 g, 15.18 mmol) in Et_2O (50 mL) was added *t*-BuLi (20.2 mL,

1.5 M in pentane, 30.3 mmol) dropwise. The reaction mixture was stirred at −90 °C for an additional 30 min and 4-bromobenzaldehyde (3.37 g, 18.21 mmol) in Et_2O (20 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and was stirred for an additional 2 h. The mixture was quenched with water and the organic phase was extracted with 1 M HCl (2 × 30 mL). The combined aqueous extracts were washed with Et_2O (30 mL), neutralized with K_2CO_3, and extracted with Et_2O (2 × 50 mL). The organic layer was dried and concentrated in vacuo, to afford **6** as a white solid. Yield: 4.96 g (87%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.42 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 7.28 (s, 2H, ArH), 7.26 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 7.13 (s, 1H, ArH), 5.74 (s, 1H, ArCH), 3.41 (s, 4H, CH_2N), 2.20 (s, 12H, NMe_2); $^{13}C\{^1H\}$ ($CDCl_3$, 50 MHz) δ: 144.5, 143.9, 138.6, 131.3, 129.2, 128.1, 126.1, 120.8 (Ar), 75.1 (CH(OH)), 64.1 (CH_2N), 45.2 (NMe_2); Anal. Calcd. for $C_{19}H_{25}BrN_2O$: C 60.48, H 6.68, N 7.42; Found: C 60.29, H 6.58, N 7.32.

5.2.2. 4-[2,6-(NMe_2CH_2)$_2$$C_6H_3$-4-CH(OTBDMS)] C_6H_4Br (7)

To a stirred solution of TBDMSCl (4.09 g, 27.16 mmol) and imidazole (3.08 g, 45.27 mmol) in THF (50 mL) was added dropwise a solution of **6** (8.54 g, 22.63 mmol) in THF (15 mL). The mixture was refluxed overnight and after cooling to room temperature methanol (3 mL) was added, followed by removal of all volatiles in vacuo. The residue was redissolved in Et_2O (50 mL), and subsequently washed with water and brine. The etheral layer was dried over $MgSO_4$, and then concentrated in vacuo to afford **7** as a yellow oil. Yield: 10.47 g (94%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.39 (d, 2H, $^3J_{HH}$ = 8.4 Hz, ArH), 7.23 (d, 2H, $^3J_{HH}$ = 8.4 Hz, ArH), 7.17 (s, 2H, ArH), 7.13 (s, 1H, ArH), 5.69 (s, 1H, ArCH), 3.44 (d, 2H, $^2J_{HH}$ = 11.4 Hz, CH_2N), 3.35 (d, 2H, $^2J_{HH}$ = 11.4 Hz, CH_2N), 2.21 (s, 12H, NMe_2), 0.89 (s, 9H, *t*-BuSi), -0.04 (d, 6H, $SiMe_2$); $^{13}C\{^1H\}$ ($CDCl_3$, 50 MHz) δ: 144.5, 144.4, 138.9, 131.1, 128.8, 127.8, 125.7, 120.5 (Ar), 76.0 (CH(OTBS)), 64.2 (CH_2N), 45.3 (NMe_2), 25.7 (C(CH_3)$_3$), 18.2 (C(CH_3)$_3$), −4.8, −4.9 ($SiMe_2$); Anal. Calcd. for $C_{25}H_{39}N_2OSi$: C 61.08, H 8.00, N 5.70; 5.71; Found: C 61.20, H 8.04, N 5.42, Si 5.60.

5.2.3. 4-[2,6-(NMe_2CH_2)$_2$$C_6H_3$-4-CH(OTBDMS)] $C_6H_4SiMe_3$ (8)

To a precooled (−78 °C) solution of **7** (1.25 g, 2.54 mmol) in Et_2O (15 mL) was added *t*-BuLi (3.4 mL, 1.5 M in pentane, 5.1 mmol) dropwise. The reaction mixture was stirred at −78 °C for an additional 30 min, and trimethylsilyl chloride (1.6 mL, 12.7 mmol) was added at once. The reaction mixture was allowed to warm to room temperature and all volatiles were evaporated in vacuo. The residue was redissolved in Et_2O (25 mL) and the solution was washed with brine. The etheral layer was dried over $MgSO_4$ and then concentrated to afford **8** as a yellow oil. Yield: 1.11 g (90%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.43 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH) 7.33 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 7.20 (s, 2H, ArH), 7.13 (s, 1H, ArH), 5.73 (s, 1H, ArCH), 3.45 (d, 2H, $^2J_{HH}$ = 11.4 Hz, CH_2N), 3.36 (d, 2H, $^2J_{HH}$ = 11.4 Hz, CH_2N), 2.21 (s, 12H, NMe_2), 0.90 (s, 9H, *t*-BuSi), 0.22 (s, 9H, $SiMe_3$), −0.04 (d, 6H, $SiMe_2$); $^{13}C\{^1H\}$ ($CDCl_3$, 50 MHz) δ: 145.8, 145.0, 138.6, 138.4, 133.1, 128.6, 126.1, 125.3 (Ar), 76.6 (CH(OTBS)), 64.3 (CH_2N), 45.3 (NMe_2), 25.8 (C(CH_3)$_3$), 18.3 (C(CH_3)$_3$), −1.1($SiMe_3$), −4.7, −4.9 ($SiMe_2$); Anal. Calcd. for $C_{28}H_{48}N_2OSi_2$: C 69.36, H 9.98, N 5.78, Si 11.58; Found: C 69.46, H 10.01, N 5.71, Si 11.39.

5.2.4. 4-[1-$SiMe_3$-2,6-(NMe_2CH_2)$_2$$C_6H_2$-4-CH(OTBDMS)]$C_6H_4SiMe_3$ (9)

n-BuLi (3.1 mL, 1.6 M in hexanes, 4.9 mmol) was added dropwise over a period of 5 min to a precooled (−78 °C) solution of **8** (2.37 g, 4.89 mmol) in hexane (20 mL). The reaction mixture was allowed to warm to room temperature and was stirred for an additional 4 h. After cooling the reaction mixture to 0 °C, a solution of trimethylsilyl trifluoromethylsulfonate (1.42 mL, 7.33 mmol) in THF (20 mL) was added dropwise over a period of 10 min and stirred for 16 h at room temperature. All volatiles were removed in vacuo and the resulting residue was extracted with hexane (3 × 50 mL). The combined hexane extracts were flushed over basic Al_2O_3 and then concentrated to afford **9** as a yellow oil. Yield: 2.49 g (91%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.42 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 7.34 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 7.32 (s, 2H, ArH), 5.74 (s, 1H, ArCH), 3.60 (d, 2H, $^2J_{HH}$ = 13.2 Hz, CH_2N), 3.40 (d, 2H, $^2J_{HH}$ = 13.2 Hz, CH_2N), 0.91 (s, 9H, *t*-BuSi), 0.33 (s, 9H, $SiMe_3$), 0.22 (s, 9H, $SiMe_3$), −0.04 (d, 6H, $SiMe_2$); $^{13}C\{^1H\}$ ($CDCl_3$, 50 MHz) δ: 146.4, 145.8, 145.0, 138.3, 137.2, 133.1, 128.0, 126.6, 126.0 (Ar), 76.5 (CH(OTBS)), 65.6 (CH_2N), 45.1 (NMe_2), 25.9 (C(CH_3)$_3$), 18.3, (C(CH_3)$_3$), 3.2 ($SiMe_3$), −1.0 ($SiMe_3$), −4.6, −4.9 ($SiMe_2$); Anal. Calcd. for $C_{31}H_{56}N_2OSi_3$: C 66.84, H 10.13, N 5.03; Found: C 66.73, H 10.29, N 4.91

5.2.5. 4-[1-$SiMe_3$-2,6-(NMe_2CH_2)$_2$$C_6H_2$-4-CH(OH)] $C_6H_4SiMe_3$ (10)

To a stirred solution of **9** (1.04 g, 1.87 mmol) in THF (15 mL) was added NBu_4F (1.9 mL, 1 M in THF, 1.9 mmol) at once. The mixture was stirred at room temperature for 1 h. All volatiles were evaporated, and the residue was extracted with hexane (3 × 100 mL). The combined fractions were washed with brine. The hexane layer was dried over $MgSO_4$ and concentrated to afford **10** as a yellow oil. Yield: 0.87 g (94%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.48 (d, 2H, $^3J_{HH}$ = 7.4 Hz, ArH), 7.38 (d, 2H, $^3J_{HH}$ = 7.4 Hz, ArH), 7.37 (s, 2H, ArH), 5.80 (s, 1H, ArCH) 3.52 (s, 4H, CH_2N), 2.11 (s, 12H, NMe_2), 0.36 (s, 9H, $SiMe_3$), 0.25 (s, 9H, $SiMe_3$); $^{13}C\{^1H\}$ ($CDCl_3$, 75 MHz) δ: 146.4, 144.9, 144.2, 139.2, 137.6, 133.4, 126.2, 125.9 (Ar), 76.1 (CH(OH)), 65.3 (CH_2N), 45.0 (NMe_2), 3.3

($SiMe_3$), −1.1 ($SiMe_3$); Anal. Calcd. for $C_{25}H_{42}N_2OSi_2$: C 67.81, H 9.56, N 6.33; Found: C 67.69, H 9.51, N 6.24.

5.2.6. [1-PdCl-2,6-(NMe_2CH_2)$_2C_6H_2$-4-CH(OH)($C_6H_4SiMe_3$)] (11)

To a suspension of **10** (1.20 g, 2.71 mmol) in freshly distilled methanol (30 mL) was added $Pd(OAc)_2$ (0.67 g, 2.98 mmol) at once. The reaction mixture was stirred for 3 h at room temperature, excess LiCl (0.75 g, 17.77 mmol) was added at once, and stirring was continued for an additional hour. All volatiles were evaporated in vacuo and the residue was extracted with dichloromethane (3 mL× 30 mL). The combined dichloromethane extracts were filtered over Celite, and removal of the volatiles afforded **11** as an orange solid. Yield: 1.23 g (89%), ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.49 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 7.35 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 6.80 (s, 2H, ArH), 5.71 (s, 1H, ArCH) 3.95 (s, 4H, CH_2N), 2.91 (s, 12H, NMe_2), 0.25 (s, 9H, $SiMe_3$). $^{13}C\{^1H\}$ ($CDCl_3$, 75 MHz) δ: 156.2, 145.3, 144.6, 140.7, 140.0, 133.8, 125.9, 118.5 (Ar), 76.6 (CH(OH)), 74.9 (CH_2N), 53.4 (NMe_2), −0.8 ($SiMe_3$); Anal. Calcd. for $C_{22}H_{33}ClN_2OPdSi$: C 51.66, H 6.50, N 5.48. Found: C 51.46, H 6.45, N 5.36.

5.2.7. [1-PdCl-2,6-(NMe_2CH_2)$_2C_6H_2$-4-CH(OAc)($C_6H_4SiMe_3$)] (12)

To a solution of **11** (155 mg, 2.71 mmol) in pyridine (1 mL) was added Ac_2O (0.5 mL) at once. The mixture was stirred at room temperature for 16 h, and subsequently poured into an ice/water mixture. The aqueous layer was extracted with dichloromethane (3×) and the combined fractions were washed with an aqueous 1 M $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated to afford **12** as a light yellow solid. Yield: 146 mg (87%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.48 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 7.29 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 6.75 (s, 2H, ArH), 6.72 (s, 1H, ArH) 3.95 (s, 4H, CH_2N), 2.91 (s, 12H, NMe_2), 2.13 (s, 3H, OAc), 0.24 (s, 9H, $SiMe_3$). $^{13}C\{^1H\}$ ($CDCl_3$, 75 MHz) δ: 170.2 (CO), 156.8, 145.3, 140.9, 140.3, 137.0, 133.7, 126.3, 119.1 (Ar), 77.4 (CHOAc), 74.9 (CH_2N), 53.3 (NMe_2), 21.6 ($COCH_3$) −0.9 ($SiMe_3$); Anal. Calcd. for $C_{24}H_{35}ClN_2O_2PdSi$: C 52.08, H 6.37, N 5.06. Found: C 51.92, H 6.31, N 4.95.

5.2.8. [1-PdCl-2,6-(NMe_2CH_2)$_2C_6H_2$-4-CH(OTBDMS)($C_6H_4SiMe_3$)] (13)

A similar procedure as described for **11** was used, with **9** as starting material (yield 92%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.43 (d, 2H, $^3J_{HH}$ = 7.5 Hz, ArH), 7.30 (d, 2H, $^3J_{HH}$ = 7.5 Hz, ArH), 6.75 (s, 2H, ArH), 5.60 (s, 1H, ArCH) 3.93 (s, 4H, CH_2N), 2.91 (s, 12H, NMe_2), 0.89 (s, 9H, *t*Bu), 0.24 (s, 9H, $SiMe_3$), −0.05, −0.07 ($SiMe_2$); $^{13}C\{^1H\}$ (acetone-d_6, 75 MHz) δ: 156.2, 146.8, 145.5, 142.1, 138.5, 133.4, 125.7, 117.7 (Ar), 77.2 (CH(OTBS)), 74.7 (CH_2N), 52.6 (NMe_2), 25.7 ($C(CH_3)_3$), 18.3 ($C(CH_3)_3$) −1.5 ($SiMe_3$), −5.1 ($SiMe_2$); Anal. Calcd. for $C_{28}H_{47}ClN_2OPdSi_2$: C 53.75, H 7.57, N 4.48; Found: C 53.60, H 7.51, N 4.33.

5.2.9. [1-PdCl-2,6-(NMe_2CH_2)$_2C_6H_2$-4-CH($C_5H_5N^+$)($C_6H_4SiMe_3$)] (14)

A solution of **11** (240 mg, 0.47 mmol) in 5 mL of pyridine was treated with chloro diethylphosphate (120 mg,0.70 mmol). The reddish solution was stirred for 16 h at room temperature. All volatiles were removed in vacuo, and the residue was redissolved in CH_2Cl_2 (50 mL). This solution was washed with water (50 mL) and brine (50 mL), and dried over $MgSO_4$. The organic layer was concentrated to 5 mL, followed by precipitation with Et_2O, to afford **14** as a orange yellow solid (277 mg, 0.40 mmol) in 85% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.18 (br d, 2H, pyridinium), 8.54 (br t, 1H, pyridinium), 8.17 (m, 2H, pyridinium), 8.16 (s, 1H, CH(NC_5H_5)), 7.47 (d, 2H, $^3J_{HH}$ = 8.1 Hz, ArH), 7.16 (d, 2H, $^3J_{HH}$ = 8.0 Hz, ArH), 6.84 (s, 2H, ArH), 3.94 (s, 4H, CH_2N), 2.85 (s, 12H, NMe_2), 0.19 (s, 9H, $SiMe_3$). $^{13}C\{^1H\}$ ($CDCl_3$, 75 MHz) δ: 146.6, 144.9, 128.8 (pyridinium), 159.7, 146.2, 142.8, 136.3, 134.6, 131.6, 127.9, 121.4 (Ar), 77.2 (CH(NC_5H_5)), 74.8 (CH_2N), 53.4 (NMe_2), −1.0 ($SiMe_3$); Anal. Calcd. for $C_{25}H_{31}Cl_2N_2PdSi$: C 53.15, H 5.53, N 4.96; Found: C 53.09, H 5.60, N 4.88.

5.3. General procedure for cationic palladium complexes 1–4

$AgBF_4$ (39 mg, 0.20 mmol) was added at once to a solution of one of the palladium halide complexes **11**–**14** (0.20 mmol) in wet acetone, resulting in the immediate precipitation of a yellowish solid. The mixture was stirred for 30 min followed by removal of all volatiles. The residue was extracted with CH_2Cl_2 (2 mL× 5 mL), and the combined extracts were filtered carefully over Celite. Evaporation of the volatiles afforded **1**–**4** as yellow to orange solids in near quantitative yields (>95%). The cationic complexes were prepared freshly prior to catalysis.

5.4. Catalyst screening

To a solution of the catalyst (1 mol%, 8 μmol) in 2.5 mL of CH_2Cl_2 or THF, was added the (substituted) benzaldehyde (0.8 mmol), *i*Pr_2EtN (10 mol% 80 μmol), and methyl isocyanoacetate (0.8 mmol). The mixture was stirred in a closed reaction vessel under ambient conditions. Samples (100 μL) for ^{1}H NMR (200 MHz) analysis were stripped from the solvent in a stream of nitrogen gas, and redissolved in $CDCl_3$ (0.5 mL). Conversions (methyl isocyanoacetate consumptions) were calculated from the intensity of the $CNCH_2COOMe$ protons versus the combined methyl ester signals.

Typically, the background reaction with benzaldehyde as substrate under these conditions, i.e. reactions run in the absence of catalyst, proceeds to 0 and 32% conversion within 6 and 24 h, respectively.

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