Preparation and characterization of the first pyrazole-based remote N-heterocyclic carbene complexes of palladium(II)

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The first pyrazolin-4-ylidene complexes of palladium(II) have been synthesized by oxidative addition of 4-iodopyrazolium salts to $Pd_2(dba)_3/PPh_3$ and were fully characterized by multi-nuclear NMR spectroscopies, ESI mass spectrometry and X-ray diffraction studies.

N-heterocyclic carbenes (NHCs) and their complexes are currently the focus of intense research in organometallic chemistry and catalysis due to their unique properties.[1] As an extension of the NHC concept, complexes bearing N-heterocyclic carbene ligands with a remote heteroatom (*r*NHC) have been reported recently. Such examples include complexes containing *r*NHC with a six-membered heterocyclic ring derived from pyridine[2] or quinoline.[2–4] Computational studies have shown that these remote carbenes are even stronger σ donors than their well-known counterparts.[2,3] Furthermore, preliminary catalytic studies have shown that palladium(II) complexes with *r*NHC ligands are more active in certain C–C coupling reactions than well-established standard NHC-containing precatalysts.[3] Despite these promising properties, *r*NHCs have not attracted the same degree of attention as standard NHCs and only few complexes with *r*NHC ligands are known.

Herein, we present the first pyrazole-derived remote carbene complexes of palladium(II) obtained by oxidative addition of 4-iodopyrazolium salts to $Pd_2(dba)_3/PPh_3$.

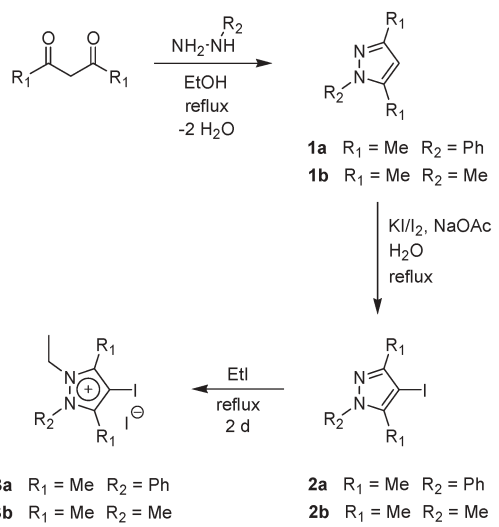
General routes to prepare palladium(II) NHC complexes include (a) *in situ* deprotonation of azolium salts with $Pd(OAc)_2$ and (b) Ag–carbene transfer method.[5] However, initial attempts to synthesize a palladium(II) pyrazolin-4-ylidene complex from a 1,2,3,5-tetrasubstituted pyrazolium salt using these methods proved unsuccessful. Apparently, the proton attached to C4 in such carbene precursors is less acidic than the C2 proton in conventional imidazolium or benzimidazolium salts. The former experiences comparatively weaker inductive effects from the electron-withdrawing N atoms, which are located 2 bonds away from the pre-carbene carbon.[6]

Due to the difficulty in deprotonating pyrazolium salts, the oxidative addition method using a low-valent metal precursor was explored.[7] Suitable ligand precursors (**3a/b**) were readily prepared in moderate yields of 33–50% by heating 1,3,5-trisubstituted-4-iodopyrazoles (**2a/b**) in neat iodoethane under reflux (Scheme 1). The former were obtained by iodination of the corresponding 1,3,5-trisubstituted pyrazoles (**1a/b**),[8] which can be generated *via* condensation of diones with monosubstituted hydrazines if not commercially available.[9] This straightforward, modular synthetic protocol allows facile fine-tuning of steric and electronic properties of the resulting *r*NHC ligands by changing various R substituents.

The formation of **3a/b** was confirmed by a base peak in the positive ESI mass spectra at *m/z* = 327 (**3a**) and 265 (**3b**), respectively, corresponding to the $[M - I]^+$ fragments. In addition, the C4 carbon atoms resonate at 72.6 ppm (**3a**, $CDCl_3$) and 69.3 ppm (**3b**, d_6-DMSO), which are shifted downfield upon N-ethylation as compared to the analogous carbon resonances for their precursors (**2a/b**) consistent with the formation of aromatic cations.

Treatment of $Pd_2(dba)_3$ with two equivalents of **3a/b** and two equivalents of triphenylphosphine in refluxing dichloromethane leads to the formation of the first palladium(II) pyrazolin-4-ylidene complexes **4a/b** (Scheme 2). Slow evaporation of a concentrated CH_2Cl_2 solution gave analytically pure **4a/b** as yellow crystals in yields of 60% and 45%, respectively. Complexes **4a/b** are stable to air and moisture. They are both soluble in polar solvents such as dichloromethane, acetonitrile or DMSO, but insoluble in pentane, diethyl ether or THF.

The formation of the complexes was confirmed by ESI mass spectrometry with positive mode spectra showing base peaks at *m/z* = 695 (**4a**) and 633 (**4b**) for the $[M - I]^+$ fragments. The phosphine donors in both complexes resonate at similar positions in ^{31}P NMR spectra with chemical shifts of 29.4 ppm (**4a**) and 29.3 ppm (**4b**), respectively. The ^1H NMR spectrum of complex **4a** shows two doublets of quartets for the two inequivalent CH_2 protons of the ethyl substituent centered at 3.78 and 3.63 ppm with



Scheme 1 Synthetic pathway for the preparation of ligand precursors.

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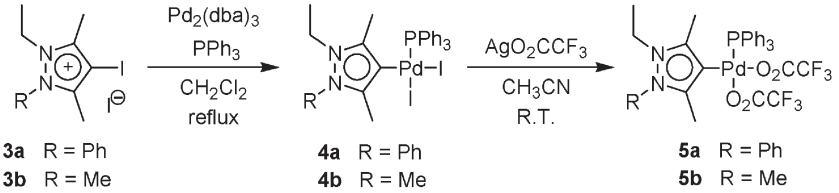

Scheme 2 Synthetic pathway for the preparation of palladium(II) pyrazolin-4-ylidene complexes.

a geminal coupling constant of $^{2}J_{(HH)}$ = 15.4 Hz. This can be attributed to a hindered rotation of the ethyl group in close proximity of the sterically bulky N-phenyl substituent. Correspondingly, the ^{13}C NMR spectrum of complex **4a** exhibits six distinct signals in the range of 132.3–127.7 ppm revealing a hindered rotation for the N-phenyl substituent as well. In contrast to **4a**, the CH_2 protons of the ethyl substituent in **4b** appear as one quartet in the ^{1}H NMR spectrum indicating a free rotation of the ethyl group neighboring to the less bulky methyl group. In addition, the carbon atoms C3 and C5 adjacent to the carbene carbon of both complexes resonate in the range of 145.4–147.2 ppm as doublets with coupling constants of $^{3}J_{(CP)}$ = 2.7–4.6 Hz, respectively. The carbenoid signals, on the other hand, were not observed due to insufficient solubilities. However, the identity of the palladium(II) pyrazolin-4-ylidene complexes **4a/b** was further confirmed by single crystal X-ray diffraction studies. Their molecular structures depicted in Fig. 1 and 2, show the expected square planar arrangement around the palladium center with the *r*NHC and the phosphine *cis* to each other. The Pd–$C_{carbene}$ bond lengths of 2.012(8) Å in **4a** and 1.996(7) Å in **4b** are comparable with those reported for standard NHC complexes or other types of *r*NHC complexes. Furthermore, the Pd–I1 bonds *trans* to the *r*NHC (2.6691(10) Å in **4a** and 2.6730(7) Å in **4b**) are slightly longer than the Pd–I2 bonds *trans* to the phosphine (2.6564(10) Å in **4a** and 2.6458(7) Å in **4b**) confirming a slightly stronger *trans* influence of the *r*NHCs. The carbene ring plane of the *r*NHC is oriented almost perpendicular to the PdI_2CP coordination plane with a torsion angle of 89.40° (**4a**) or 85.98° (**4b**) to minimize interligand interactions.

In order to improve the solubilities of the new palladium(II) pyrazolin-4-ylidene complexes, which would help in identifying the carbene signals by ^{13}C NMR spectroscopy, we substituted the iodo ligands of complexes **4a/b** by trifluoroacetato ligands according to a literature method (Scheme 2).[10] The dicarboxylato complexes **5a/b** were obtained as colorless crystals in yields of 70% and 68%, respectively, by slow evaporation of concentrated CH_2Cl_2–hexane solutions. They are well soluble in chlorinated solvents, acetonitrile, and DMSO, but insoluble in nonpolar solvents such as hexane, toluene and diethyl ether. Under aerobic conditions and upon prolonged standing, solutions of both complexes **5a/b** slowly deposit palladium black. A similar behavior has been observed for mixed dicarboxylato–NHC complexes derived from imidazole and benzimidazole as well.[10] The ^{1}H and ^{31}P NMR spectra of complexes **5a/b** show little changes in their chemical shifts compared to those for their precursor complexes **4a/b**. However, ^{19}F NMR (external standard: CF_3CO_2H) spectroscopy on **5a/b** reveals two singlets in a narrow range of 0.70 to −0.05 ppm, pointing to a *cis* arrangement of the carboxylato ligands in solution. In addtition, the ^{13}C carbene signals of **5a** and **5b** arise as doublets at 115.1 ppm with $^{2}J_{(CP)}$ = 10.4 Hz and at 113.8 ppm with $^{2}J_{(CP)}$ = 9.9 Hz, respectively. It is worth mentioning, that these carbene signals are significantly shifted to lower field by 42.5 and 44.5 ppm with reference to the analogous C4 carbon resonances in their ligand precursors **3a/b**. Finally, two broad quartets are observed at 160.5 ppm with $^{2}J_{(CF)}$ = 31.8 Hz and at 116.3 ppm with $^{1}J_{(CF)}$ = 273.9 Hz for the CO and CF_3 carbon atoms of complex **5a**, respectively. Similar signals for the trifluoroacetato ligands are also observed for complex **5b**.

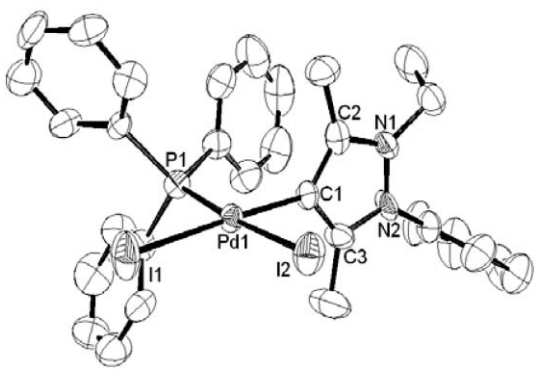

Fig. 1 Molecular structure of **4a** showing 50% probability ellipsoids. Selected bond lengths[Å] and angles [°]: Pd1–C1 2.012(8), Pd1–P1 2.266(3), Pd1–I1 2.6691(10), Pd1–I2 2.6564(10), C1–C2 1.381(13), C1–C3 1.373(13), N1–C2 1.358(12), N2–C3 1.366(12), N1–N2 1.358(11); C1–Pd1–P1 90.6(3), C1–Pd1–I2 86.1(3), P1–Pd1–I1 91.67(7), I2–Pd1–I1 91.69(3), C3–C1–C2 106.0(8).

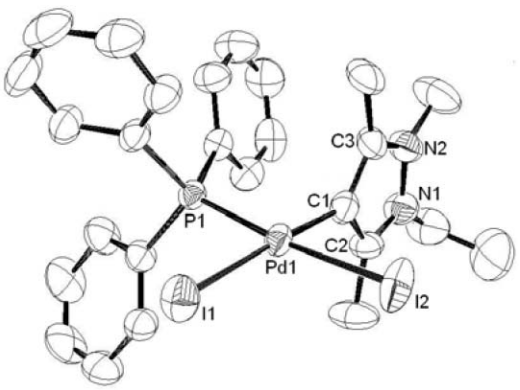

Fig. 2 Molecular structure of **4b** showing 50% probability ellipsoids. Selected bond lengths[Å] and angles [°]: Pd1–C1 1.996(7), Pd1–P1 2.2765(16), Pd1–I1 2.6730(7), Pd1–I2 2.6458(7), C1–C2 1.377(9), C1–C3 1.388(9), N1–C2 1.330(9), N2–C3 1.348(9), N1–N2 1.359(8); C1–Pd1–P1 89.79(19), C1–Pd1–I2 86.44(18), P1–Pd1–I1 90.69(4), I2–Pd1–I1 93.35(2), C3–C1–C2 104.3(6).

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In conclusion, we have presented a straightforward synthesis of unprecedented palladium(II) pyrazolin-4-ylidene complexes by oxidative addition of 4-iodopyrazolium salts to $Pd_2(dba)_3/PPh_3$. Studies to explore the catalytic activities of these complexes for C–C coupling reactions and to gain a better understanding of these unique ligands are ongoing.

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Notes and references

† *Crystal data*: **4a**·0.5toluene: $C_{34.5}H_{35}I_2N_2PPd$, M = 868.82, monoclinic, a = 9.3123(4), b = 16.8404(7), c = 21.6379(9) Å, β = 95.719(1), U = 3376.4(2) Å^3, T = 295(2) K, space group $P2(1)/c$, Z = 4, D_c = 1.709 g cm^{-1}, μ (Mo-K$_\alpha$) = 2.451 mm^{-1}, 19717 reflections measured, 5935 unique (R_{int}= 0.0657) which were used in all calculations. The final wR^2 was 0.1548 (all data).

4b·0.5CH_2Cl_2: $C_{26.50}H_{30}ClI_2N_2PPd$, M = 803.14, monoclinic, a = 9.3019(5), b = 16.8771(9), c = 18.9728(9) Å, β = 94.530(1), U = 2969.2(3) Å^3, T = 295(2) K, space group $P2(1)/c$, Z = 4, D_c = 1.797 g cm^{-1}, μ (Mo-K$_\alpha$) = 2.865 mm^{-1}, 20857 reflections measured, 6797 unique (R_{int} = 0.0357) which were used in all calculations. The final wR^2 was 0.1573 (all data).

‡ *Spectroscopic data*: **3a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81–7.65 (m, 5 H, Ar–H), 4.39 (m, $^3J_{(H,H)}$ = 7.3 Hz, 2 H, CH_2), 2.70 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 1.22 (t, $^3J_{(H,H)}$ = 7.3 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ NMR (75.47 MHz, $CDCl_3$): 149.9, 149.8 (s, CCH_3), 133.6, 131.8, 131.6, 129.8 (s, Ar–C), 72.6 (s, CI), 46.7 (s, CH_2), 15.4 (s, CCH_3), 15.0 (s, CH_2CH_3). **3b**: ^{1}H NMR (300 MHz, d_6-DMSO): δ 4.54 (m, $^3J_{(H,H)}$ = 7.2 Hz, 2 H, CH_2), 4.03 (s, NCH_3), 2.49 (s, 3 H, CH_3), 2.45 (s, 3 H, CH_3), 1.30 (t, $^3J_{(H,H)}$ = 7.2 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ NMR (75.47 MHz, d_6-DMSO): 147.9, 146.8 (s, CCH_3), 69.3 (s, CI), 43.2 (s, CH_2), 35.1 (s, NCH_3), 13.7, 13.2 (s, CCH_3), 12.8 (s, CH_2CH_3). **4a**: ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.78–6.87 (m, 20 H, Ar–H), 3.78 (m, $^2J_{(H,H)}$ = 15.4 Hz, $^3J_{(H,H)}$ = 7.2 Hz, 1 H, CH_2), 3.63 (m, $^2J_{(H,H)}$ = 15.4 Hz, $^3J_{(H,H)}$ = 7.2 Hz, 1 H, CH_2), 2.36 (s, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 0.95 (m, $^3J_{(H,H)}$ = 7.2 Hz, 3 H, CH_2CH_3). ^{31}P NMR (121 MHz, CD_2Cl_2): 29.4 (s, 1 P, PPh_3). $^{13}C\{^1H\}$ NMR (75.47 MHz, CD_2Cl_2): 147.2 (d, $^3J_{(P,C)}$ = 3.8 Hz, CCH_3), 146.9 (d, $^3J_{(P,C)}$ = 2.7 Hz, CCH_3), 134.9 (d, $^{2/3}J_{(P,C)}$ = 11.0 Hz, Ar–C), 132.9 (d, $^1J_{(P,C)}$ = 48.3 Hz, Ar–C), 132.3, 131.6, 130.5 (s, Ar–C), 130.2 (d, $^4J_{(P,C)}$ = 2.2 Hz, Ar–C), 130.1, 128.7, 127.8 (s, Ar–C), 127.7 (d, $^{2/3}J_{(P,C)}$ = 11.0 Hz, Ar–C), 41.9 (s, CH_2), 15.3, 15.1 (s, CCH_3), 14.7 (s, CH_2CH_3). **4b**: ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.68–7.30 (m, 15 H, Ar–H), 3.86 (m, $^3J_{(H,H)}$ = 7.3 Hz, 2 H, CH_2), 3.43 (s, 3 H, NCH_3), 2.21 (s, 3 H, CH_3), 2.13 (s, 3 H, CH_3), 1.15 (t, $^3J_{(H,H)}$ = 7.3 Hz, 3 H, CH_2CH_3). ^{31}P NMR (121 MHz, CD_2Cl_2): 29.3 (s, 1 P, PPh_3). $^{13}C\{^1H\}$ NMR (125.76 MHz, CD_2Cl_2): 145.9 (d, $^3J_{(P,C)}$ = 4.6 Hz, CCH_3), 145.4 (d, $^3J_{(P,C)}$ = 3.7 Hz, CCH_3), 135.0 (d, $^{2/3}J_{(P,C)}$ = 11.0 Hz, Ar–C), 132.7 (d, $^1J_{(P,C)}$ = 48.6 Hz, Ar–C), 130.2 (d, $^4J_{(P,C)}$ = 1.8 Hz, Ar–C), 127.7 (d, $^{2/3}J_{(P,C)}$ = 11.0 Hz, Ar–C), 41.6 (s, CH_2), 33.2 (s, NCH_3), 15.0, 14.9 (s, CCH_3), 14.7 (s, CH_2CH_3). **5a**: ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.74–6.94 (m, 20 H, Ar–H), 3.82 (m, $^2J_{(H,H)}$ = 15.0 Hz, $^3J_{(H,H)}$ = 7.2 Hz, 1 H, CH_2), 3.69 (m, $^2J_{(H,H)}$ = 15.0 Hz, $^3J_{(H,H)}$ = 7.2 Hz, 1 H, CH_2), 2.42 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 0.95 (m, $^3J_{(H,H)}$ = 7.2 Hz, 3 H, CH_2CH_3). ^{31}P NMR (121 MHz, CD_2Cl_2): 29.8 (s, 1 P, PPh_3). ^{19}F NMR (282 MHz, CD_2Cl_2): 0.58, −0.04 (s, CF_3). $^{13}C\{^1H\}$ NMR (75.47 MHz, CD_2Cl_2): 160.5 (m, $^3J_{(F,C)}$ = 31.8 Hz, CO), 148.9 (d, $^3J_{(P,C)}$ = 2.7 Hz, CCH_3), 148.4 (d, $^3J_{(P,C)}$ = 2.7 Hz, CCH_3), 134.3 (d, $^{2/3}J_{(P,C)}$ = 11.5 Hz, Ar–C), 132.0, 131.9 (s, Ar–C), 131.1 (d, $^4J_{(P,C)}$ = 2.7 Hz, Ar–C), 130.7, 130.3 (s, Ar–C), 129.1 (d, $^1J_{(P,C)}$ = 55.4 Hz, Ar–C), 128.4 (s, Ar–C), 128.3 (d, $^{2/3}J_{(P,C)}$ = 11.5 Hz, Ar–C), 127.7 (s, Ar–C), 116.3 (m, $^1J_{(F,C)}$ = 273.9 Hz, CF_3), 115.1 (d, $^2J_{(P,C)}$ = 10.4 Hz, $C_{carbene}$), 42.0 (s, CH_2), 14.4, 14.2 (s, CCH_3), 13.9 (s, CH_2CH_3). **5b**: ^{1}H NMR (300 MHz, CD_2Cl_2): δ 7.66–7.38 (m, 15 H, Ar–H), 3.99 (m, 2 H, CH_2), 3.55 (s, 3 H, NCH_3), 2.27 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 1.17 (m, $^3J_{(H,H)}$ = 7.2 Hz, 3 H, CH_2CH_3). ^{31}P NMR (121 MHz, CD_2Cl_2): 29.4 (s, 1 P, PPh_3). ^{19}F NMR (282 MHz, CD_2Cl_2): 0.65, −0.04 (s, CF_3). $^{13}C\{^1H\}$ NMR (75.47 MHz, CD_2Cl_2): 160.4 (m, $^3J_{(F,C)}$ = 34.4 Hz, CO), 147.7 (d, $^3J_{(P,C)}$ = 3.3 Hz, CCH_3), 146.8 (d, $^3J_{(P,C)}$ = 2.7 Hz, CCH_3), 134.3 (d, $^{2/3}J_{(P,C)}$ = 11.0 Hz, Ar–C), 131.0 (d, $^4J_{(P,C)}$ = 2.2 Hz, Ar–C), 128.9 (d, $^1J_{(P,C)}$= 54.9 Hz, Ar–C), 128.1 (d, $^{2/3}J_{(P,C)}$ = 11.0 Hz, Ar–C), 116.3 (m, $^1J_{(F,C)}$ = 290.9 Hz, CF_3), 113.8 (d, $^2J_{(P,C)}$ = 9.9 Hz, $C_{carbene}$), 41.5 (s, CH_2), 33.1 (s, NCH_3), 14.2, 13.9 (s, CCH_3), 13.6 (s, CH_2CH_3).

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