

Catalytically active palladium pyridylidene complexes: pyridinium ionic liquids as *N*-heterocyclic carbene precursors

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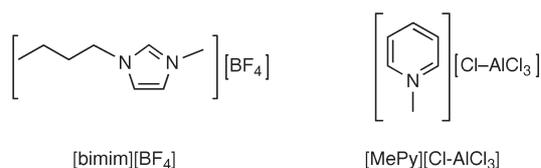
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Pyridinium salts similar to those used as ionic liquid solvents readily undergo palladation in the presence of a base, thus giving palladium-pyridylidene *N*-heterocyclic carbene complexes that are active catalysts for Suzuki-type cross-coupling reactions.

Solvents are generally used to maximize the homogeneous distribution of reaction partners and to control and balance temperature effects throughout a reaction. In addition, they may accelerate reactions by stabilizing key transition states along the reaction coordinate through non-covalent interactions. However, they are considered to be chemically inert during reactions, that is, they are not subject to breaking and making of (covalent) bonds.

Recently, ionic liquids have been promoted as a novel class of solvents,¹ since they combine a variety of advantages such as environmental friendliness (virtually no vapor pressure, easiness of recovery and recycling), physical robustness within a large temperature range, and high solubilization potential, *e.g.*, for reactions catalyzed by metal nanoparticles.² Most often, ionic liquids derived from imidazolium and pyridinium ions have been used, for example [bimim][BF₄] and [MePy][Cl–AlCl₃].

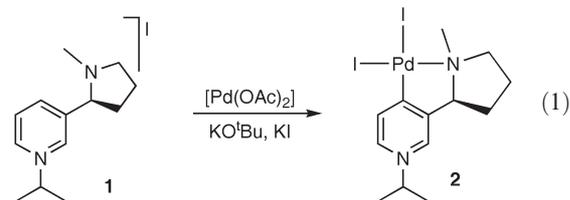


Interestingly, imidazolium ionic liquids have also been used as precursors of *N*-heterocyclic carbene ligands in organometallic chemistry.³ It has been shown that metallation of imidazolium salts can occur under mild conditions and in the absence of a base.⁴ These findings suggest that ionic liquids may act as reagents and not only as solvents in transition metal catalyzed reactions.

In contrast to imidazolium salts, pyridinium ionic liquids have been assumed to be resistant towards metallation.⁵ Their resistance can be rationalized by a comparatively low stabilization of the corresponding carbene by one nitrogen only. However, pyridylidene-type transition metal complexes have been proposed as products from *N*-protonation and -alkylation of platinum group pyridyl complexes.⁶ In addition, similar complexes have

recently been shown to display remarkably strong *trans* effects.⁷ Here, we provide evidence for the formation of pyridylidene complexes using pyridinium ionic liquids as ligand precursors. Moreover these pyridylidene complexes actively catalyze Suzuki cross-coupling reactions.

Our approach towards pyridylidene complexes starts from nicotine as a versatile starting material. First, coordination of the pyrrolidine nitrogen should support the M–C_{carbene} bond through chelate formation. Second, enantiopure nicotine is readily available and offers a cheap and convenient access to chiral complexes that may be useful for asymmetric catalysis. Thus, the pyridinium salt **1** has been prepared from nicotine by selective alkylation of the imine nitrogen with *i*PrI. At room temperature, **1** is a highly viscous ionic liquid that dissolves readily in alcohols, though only sparingly in THF and H₂O. Palladation of **1** occurs smoothly at room temperature in the presence of [Pd(OAc)₂] and a base such as KO^tBu (eqn. 1).



Contrary to our expectation, metallation takes place at the 4- rather than at the most acidic 2-pyridinium position, thus affording the palladium complex **2** as an orange solid.† The observed regioselectivity of metallation possibly originates from the directing effects of the pyrrolidine substituent,⁸ though shielding of the *ortho* positions by the bulky isopropyl groups may also be effective.

The two low-field doublets at δ 8.69 and 8.49 in the ¹H NMR spectrum of **2** are indicative for the protons *ortho* to the pyridine nitrogen and are therefore diagnostic for the site of metallation. Notably, we observed a long-range coupling between H² and H⁵ (³J_{HH} = 1.7 Hz) that is relatively large, probably owing to the particular electronic configuration of the heterocycle.

The proposed structure of **2** was unequivocally confirmed by an X-ray diffraction analysis‡ of single crystals that were grown by slow diffusion of Et₂O into a DMSO solution of **2**. The unit cell contains four independent molecules of **2**, whose structures are mutually strongly related. The molecular structure (Fig. 1) reveals a palladium center in a slightly distorted square-planar environment defined by two iodide ligands and the *C,N*-bidentate chelating pyridylidene ligand. The most relevant features of the five-membered palladacycle—average bite angle 82.5(2)°, Pd–C 1.975(5) Å, Pd–N 2.136(4) Å—are very similar to those of related

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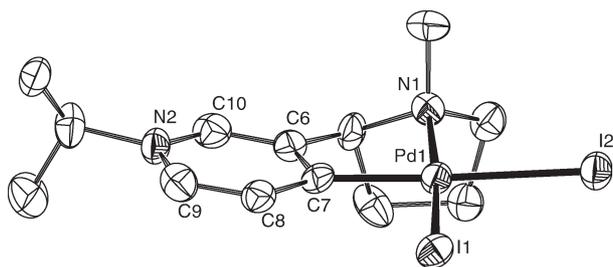
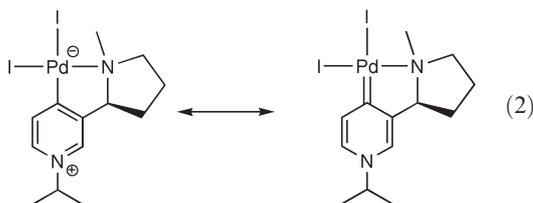


Fig. 1 ORTEP representation of **2** (one of the four independent molecules) with thermal ellipsoids at the 30% probability level, hydrogen atoms are omitted. Pertinent bond lengths (Å) and angles (°): Pd1–C7 1.994(10), Pd1–N1 2.129(8), Pd1–I1 2.587(1), Pd1–I2 2.683(1); C7–Pd1–N1 82.6(4), C7–Pd1–I1 93.2(3), C7–Pd1–I2 175.2(3), N1–Pd1–I1 173.5(2), I1–Pd1–I2 91.64(3).

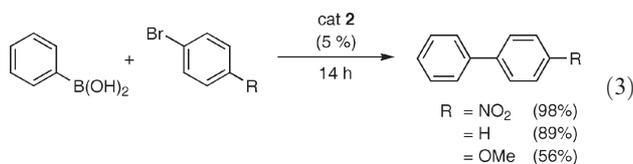
chelating arylamine palladium complexes.⁹ Apparently, the metal–carbon bond length in these complexes is essentially defined by the chelating amine site. Hence, Pd–C bond analysis does not provide any information on the metal–carbon bond strength. In contrast, the metal–iodide bonds represent useful probes for the *trans* influence of the pyridylidene site. The Pd–I bond *trans* to carbon (average Pd1–I2 2.692(1) Å) is significantly longer than the one *trans* to nitrogen (average Pd1–N1 2.589(1) Å). The difference of 0.10 Å corresponds to a 3.7% bond stretching and indicates a *trans* influence of the pyridylidene ligand that is about as strong as the one observed in related imidazolylidene complexes.¹⁰

The pyridinium ring does not show any significant C–C bond length alterations that could indicate a quinoidal pyridylidene structure in the solid state (eqn. 2). Conservation of the sp² hybridization at the pyridine nitrogen would point to a zwitterionic structure with a highly dipolar resonance form, comprising a cationic pyridinium group and an anionic palladate rather than a neutral pyridylidene palladium complex (eqn. 2).



The ¹³C NMR chemical shift of the palladium-bound carbon (δ_C 176.2), however, compares well with related heterocyclic carbenes^{6,7} and suggests considerable carbene contribution to the bonding.

The pyridylidene complex **2** actively catalyzes the Suzuki coupling of aryl iodides and bromides with phenylboronic acids (eqn. 3).§



Conversions typically reach completion after 24 h, which compares well with similar catalytic experiments performed with palladium salts in pyridinium ionic liquids.⁵ Addition of Hg⁰ to the reaction mixture gives 70% conversion, which shows that the reaction is at least predominantly homogeneous.^{11,12} Deactivated

aryl bromides such as 4-bromoanisole are converted significantly slower (56% after 24 h) and aryl chlorides essentially fail (11%), though optimization of reaction conditions may improve catalyst performance.

In conclusion, our results show that stable *N*-heterocyclic carbene complexes are readily accessible from pyridinium salts by base-promoted palladation. In view of the mild conditions for the formation of these novel palladium complexes and their activity in cross-coupling reactions, similar pyridylidene palladium complexes may be responsible for the observed catalytic activity when using palladium as catalyst precursor in pyridinium ionic liquids. Moreover, we have disclosed a new and cheap entry to chiral carbene complexes. Their performance in asymmetric catalysis is currently under investigation and will be reported in due course.

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Notes and references

† Synthesis of **2**: To a suspension of pyridinium salt **1** (0.81 g, 2.4 mmol) in dry THF (20 mL) was added KO^tBu (0.27 g, 2.4 mmol) followed by Pd(OAc)₂ (0.55 g, 2.4 mmol). After 1 h, KI (1.66 g, 10 mmol) was added and the mixture was stirred for 2 d at room temperature. Volatiles were evaporated *in vacuo*, and the residue was purified by column chromatography (SiO₂, CH₂Cl₂/acetone 8 : 1). The orange fraction was collected and evaporated to yield **2** as an orange solid (0.36 g, 27%). An analytically pure sample of **2** was obtained by recrystallization from CH₂Cl₂ and pentane. Anal. found (calcd) for C₁₃H₂₀I₂N₂Pd (564.54): C 27.67 (27.66), H 3.65 (3.57); N 4.91 (4.96); Pd 18.83 (18.85). ¹H NMR (500 MHz, DMSO-*d*₆, 298 K) δ 8.69 (1H, d, ³J = 6.4 Hz, H⁶), 8.49 (1H, d, ³J = 1.7 Hz, H²), 8.27 (1H, dd, ³J = 6.5 Hz, ⁴J = 1.7 Hz, H³), 4.71 (1H, sept, ³J = 6.7 Hz, CHMe₂), 4.3 (1H, br, NCHH), 4.09 (1H, t, ³J = 8.5 Hz, pyCHN), 3.74 (s, 3H, NCH₃), 2.53 (2H, m, NCHH, NCH₂CH₂CHH), 2.4 (1H, m, NCH₂CHH), 2.0 (2H, m, NCH₂CHH, NCH₂CH₂CHH), 1.55 (3H, d, ³J = 6.7 Hz, CHMeCH₃), 1.54 (3H, d, ³J = 6.7 Hz, CHCH₃Me); ¹³C {¹H} NMR (125 MHz, DMSO-*d*₆, 353 K) δ 176.2 (C–Pd), 155.2 (C³), 140.0 (C⁵), 135.7 (C⁶), 132.0 (C²), 76.5 (pyCN), 62.0 (CHMe₂), 61.7 (br, NCH₂), 47.3 (NCH₃), 34.3 (NCH₂CH₂CH₂), 22.3 (CHCH₃Me), 22.2 (CHMeCH₃), 21.8 (NCH₂CH₂).

‡ Crystal data for **2**: Empirical formula [C₁₃H₂₀I₂N₂Pd], *M* 564.51, orange rod, orthorhombic, space group *P*2₁2₁2₁ (no. 19), *a* = 12.7386(6), *b* = 16.3024(8), *c* = 31.923(2) Å, *V* = 6629.4(6) Å³, *Z* = 16, *D*_c = 2.262 g cm⁻³, MoK α radiation, λ = 0.71073 Å, *T* = 153(2) K, 2 θ _{max} = 52.2°, 50877 reflections measured, 13031 unique (*R*_{int} = 0.0882). Final *Goof* = 0.944, *RI* = 0.0423, *wRI* = 0.0853, *R* indices based on 9801 reflections with *I* > 2 σ (*I*) (refinement on *F*²), 661 parameters, 0 restraints, Flack parameter = 0.01(3). Lp and absorption corrections applied, μ = 4.832 mm⁻¹. CCDC 275134. See <http://dx.doi.org/10.1039/b508225k> for crystallographic data in CIF or other electronic format.

§ General Suzuki procedure: To a solution of phenylboronic acid (0.55 mmol) and aryl bromide (0.50 mmol) in DMSO (3.0 mL) were added bis(ethylene glycol) dibutyl ether (0.25 mmol, ¹H NMR standard) and aqueous K₂CO₃ (1.2 mmol dissolved in 1.2 mL H₂O), followed by **2** (100 mg, 25 μ mol) as a DMSO solution (2.5 mmol in 10 g DMSO). The reaction mixture was stirred at 100 °C. Aliquots were taken from the reaction mixture, suspended into aqueous KOH (5 mL) and extracted with Et₂O (3 \times 5 mL). The combined organic fractions were washed with brine (8 mL), dried (Na₂SO₄), and evaporated to dryness. The residue was filtered through a short pad of SiO₂ (Et₂O as eluent), evaporated to dryness, and analyzed by ¹H NMR.

- 1 T. Welton, *Chem. Rev.*, 1999, **99**, 2071; P. Wasserscheid and W. Keim, *Angew. Chem., Int. Ed.*, 2000, **39**, 3772; J. Dupont, R. T. de Souza and P. A. Z. Suarez, *Chem. Rev.*, 2002, **102**, 3667.
- 2 C. C. Cassol, A. P. Umpierre, G. Machado, S. I. Wolke and J. Dupont, *J. Am. Chem. Soc.*, 2005, **127**, 3298.
- 3 D. Bourissou, O. Guerret, F. P. Gabbaï and G. Bertrand, *Chem. Rev.*, 2000, **100**, 39; W. A. Herrmann, *Angew. Chem., Int. Ed.*, 2002, **41**, 1290.

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- 4 S. Gründemann, M. Albrecht, A. Kovacevic, J. W. Faller and R. H. Crabtree, *J. Chem. Soc., Dalton Trans.*, 2002, 2163; D. S. McGuinness, K. J. Cavell, B. F. Yates, B. W. Skelton and A. H. White, *J. Am. Chem. Soc.*, 2001, **123**, 8317.
 - 5 D. Zhao, Z. Fei, T. J. Geldbach, R. Scopelliti and P. Dyson, *J. Am. Chem. Soc.*, 2004, **126**, 15876.
 - 6 B. Crociani, F. Di Bianca, A. Gioenco and A. Scrivanti, *J. Organomet. Chem.*, 1983, **251**, 393; B. Crociani, F. Di Bianca, A. Gioenco and A. Scrivanti, *J. Organomet. Chem.*, 1986, **269**, 295; G. R. Newkome, D. W. Evans and F. R. Fronczek, *Inorg. Chem.*, 1987, **26**, 3500.
 - 7 J. S. Owen, J. A. Labinger and J. E. Bercaw, *J. Am. Chem. Soc.*, 2004, **126**, 8247.
 - 8 A. J. Meyers and R. A. Gabel, *J. Org. Chem.*, 1982, **47**, 2633.
 - 9 For examples, see: J.-M. Valk, F. Maassarani, P. van der Sluis, A. L. Spek, J. Boersma and G. van Koten, *Organometallics*, 1994, **13**, 2320; G. LeBorgne, S. E. Bouaoud, D. Grandjean, P. Braunstein, J. Dehand and M. Pfeffer, *J. Organomet. Chem.*, 1977, **136**, 375.
 - 10 J. A. Loch, M. Albrecht, E. Peris, J. W. Faller and R. H. Crabtree, *Organometallics*, 2002, **21**, 700.
 - 11 D. R. Anton and R. H. Crabtree, *Organometallics*, 1983, **2**, 855.
 - 12 Heterogeneous Pd has been reported to catalyze Suzuki reactions. For examples, see: J. Tsuji, *Palladium Reagents and Catalysts*, Wiley-VCH, Weinheim, 2004, p. 293.