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N-Acylamidine Palladium(II) Complexes. Synthesis, Structures, and Catalytic Activity for Suzuki−Miyaura Cross-Coupling Reactions: Experiments and DFT Calculations

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N-Acylamidines **2** are easily prepared by acylation of amidines **1**. Upon treatment with $PdCl_2(PhCN)_2$, they form 2:1 $PdCl_2$ complexes **3** with trans configuration, acting as monodentate ligands via the nitrogen atom remote from the carbonyl group. The structures of the complexes **3a**−**c** in the solid state were obtained by X-ray crystallography. As studied by DFT calculations on 2:1 model complexes, many isomeric structures **6** with different conformations and configurations are associated with local minima on the energy hyperface within an energy range of 4 kcal/mol. The complexes **3** show very high catalytic activity in Suzuki−Miyaura cross-coupling reactions, either as isolated crystals or prepared in situ without isolation.

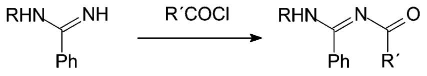
Introduction

In recent years, ligands offering nitrogen lone pairs as sites for metal complexation have found increasing interest in organometallic chemistry, especially because of their superior properties in catalysis.[1−3] *N*-Acylamidines **2** appeared to us to be interesting ligands for metal complexation due to their chemical resemblance to β-dialkylaminoacroleine derivatives (enaminones),[4] which have found applications in coordination chemistry.[5] In comparison to those, we envisaged altered electronic properties of *N*-acylamidines **2** due to the nitrogen atom in the 3-position which may well have influence on the reactivity of these ligands toward metal ions. Earlier work of our group in this field included copper(II) complexes, which display rather versatile coordination chemistry, depending on stoichiometry, charge on ligands, and solvent properties.[6]

Here, we present our experimental and theoretical results concerning the complexation of variably substituted *N*-acylamidine ligands **2** toward palladium(II), the structures of the complexes obtained as well as their catalytic properties in Suzuki−Miyaura cross-coupling reactions. We supplement our experimental results by DFT model calculations on 1:1 and 2:1 Pd(II) complexes.

Synthesis

N-Acylamidines **2** are easily prepared by acylation of the corresponding secondary amidines **1** with acyl chlorides in 66−97% yield.[7] In these reactions, basic (2 N NaOH) aqueous solutions of amidines are treated with solutions of the acyl chloride in acetone as solvent. Secondary *N*-acylamidines **2** are subject to tautomerism. Spectroscopic data as well as a crystal structure determination (see below and the Supporting Information) show that the tautomer with adjacent C═O and C═N bonds predominates in the equilibrium mixtures.



1 **2**

	R	R´	
2a	*n*Pr	*t*Bu	66 %
2b	*n*Pr	*p*Tol	89 %
2c	*n*Bu	*t*Bu	85 %
2d	*n*Bu	Ph	88 %
2e	*t*Bu	*t*Bu	97 %
2f	*t*Bu	*p*Tol	88 %

Palladium(II) complexes **3** of *N*-acylamidines **2** are synthesized as crystalline materials by dissolving 1 equiv of bis(benzonitrile)palladium(II) dichloride and 2 equiv of the ligand **2** in dichloromethane or chloroform. Careful addition of diethyl ether to form an upper layer results in the formation of yellow single crystals, which are collected after a couple of days in 70−89% yield. Com-

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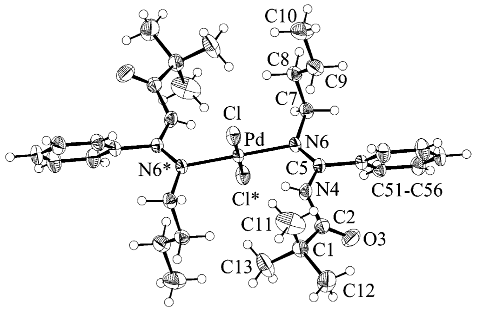
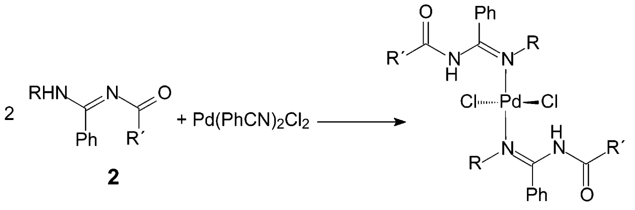


FIGURE 1. Molecular structure of **3a** in the solid state (X-ray).

pounds **3** are all stable in air, nonhygroscopic, and decompose only at temperatures above 200 °C.



3

	R	R′	
3a	*n*Bu	*t*Bu	89 %
3b	*n*Pr	*t*Bu	81 %
3c	*n*Pr	*p*Tol	70 %

X-ray Diffraction Studies

The structure of **2f** in the solid state was determined by X-ray crystallography. **2f** crystallizes as the tautomer with the mobile proton at nitrogen atom N5, remote from the carbonyl group (see the Supporting Information for the figure and structural data). The resulting O=C−N=C fragment adopts a *cisoid* gauche conformation (torsional angle −20.54°), as is often observed in *N*-acylimine derivatives.[8,9] The bond lengths along O1−C2−N3−C4−N5 indicate substantial π-interaction (1.236, 1.355, 1.314, 1.325 Å). The spacious *tert*-butyl group is positioned in the endo position.

According to the X-ray diffraction studies of the Pd(II) complexes **3a**, **3b**, and **3c**, all three compounds crystallize as 2:1 trans isomers. $PdCl_2(PhCN)_2$, used for the complexation experiments, also has trans configuration.[10] The ligands adopt a head to tail orientation with respect to each other (see Figure 1). They are substantially twisted out of the plane of the tetracoordinate planar Pd(II) center, which occupies the crystallographic center of symmetry. In all examples, we observe a monodentate coordination of the ligand to palladium(II) using the nitrogen atom remote from the acyl group as the donor atom, contrary to the Cu(II) complexes, where *N*-acylamidines act as chelating ligands.[6] During the complexation, hydrogen shift from the nitrogen atom remote from carbonyl to the other nitrogen atom takes place.

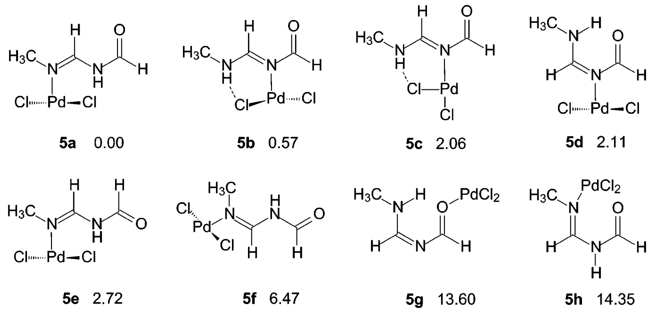


FIGURE 2. Relative energies (kcal/mol) for 1:1 model complexes **5** (B3LYP-DFT results including ZPE).

DFT Model Calculations

N-Acylamidines **2** offer principally three coordination sites for metal complexation, the carbonyl oxygen atom and the two nitrogen atoms. By adopting a U-shape configuration, bidentate binding producing a chelate type complex is possible as shown for several Cu(II) complexes.[6] DFT calculations on *N*-formyl-*N′*-methylamidine ($CH_3NHCH{=}NCHO$) **4** as model ligand were performed using the DFT functional B3LYP (Becke's three-parameter hybrid functional using the LYP (Lee, Yang, Parr) correlation functional) and the ECP basis set LANL2DZ[11] augmented with f-functions[12] for Pd and 6-31+G(d,p) for C, H, N, O as implemented in the program package GAUSSIAN 98, A.6.[13] The results obtained (Figures 2 and 3) include zero-point correction (ZPE).

First, with respect to the previously described copper complexes,[6] various 1:1 complexes of **4** and $PdCl_2$ were calculated to investigate the propensity of the different coordination sites for $PdCl_2$ complexation (Figure 2). From these calculations, one can derive that both nitrogen atoms of *N*-acylamidines **2**/**4** may serve as complexation sites for Pd(II) ions with a small preference for complexation at the nitrogen atom remote from the carbonyl group (**5a**) over **5b**. According to charges (NBO: −0.618 e versus −0.655 e) and HOMO coefficients, this nitrogen atom presents the softer of the two nitrogen donor centers in the sense of Pearson's[14] hard−soft principle. Both isomers have *s-cis*-carbonyl arrangements. Indeed, configuration and conformation of the ligand play a vital role for the relative energy of the complexes. More energy rich are all-trans isomers (**5e**,**f**) and U-shaped forms (**5d**,**g**,**h**). As expected for Pd(II),

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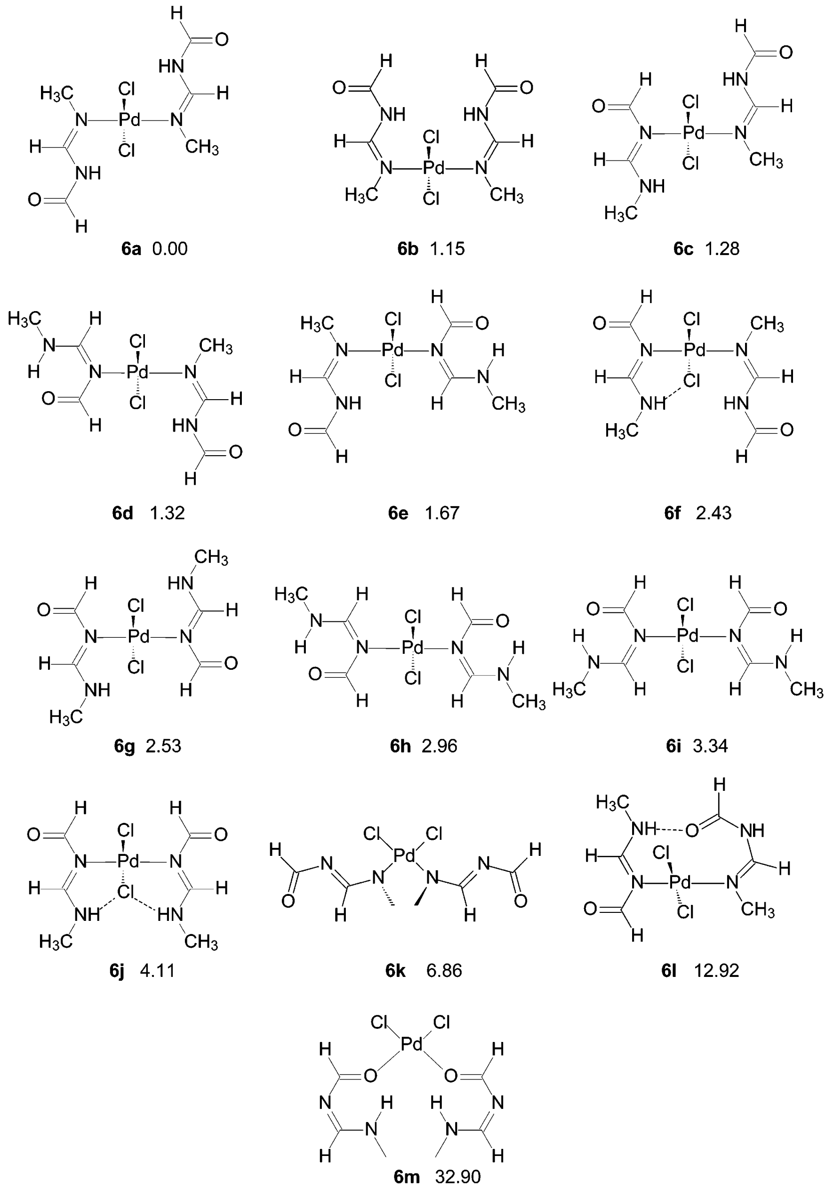

FIGURE 3. Relative energies (kcal/mol) for 2:1 model complexes **6** (B3LYP-DFT results including ZPE).

complexation on oxygen is disfavored (**5g**). Even geometrically possible formation of a chelate form is strongly avoided (**5h**), monodentate nitrogen coordination predominates instead (O−Pd distance: 2.82 Å, N−Pd 2.01 Å). Thus, Pd(II) behaves very differently from Cu(II), which prefers 1:1 complexation giving chelate complexes with ligand configuration as in **5h**.[6] The complexation energy for the formation of **5a** (calculated from **4** and $PdCl_2$ without considering basis set superposition errors (BSSE[15])) amounts to 38.5 kcal/mol.

With these results in hand, we expanded our theoretical investigations toward 2:1 complexes **6** of model *N*-acylamidine **4**, which have the same composition as the experimentally observed compounds (Figure 3). We localized 10 minima, which are less than 4.2 kcal/mol apart from each other. The lowest total energy is predicted for the centrosymmetric isomer **6a**, which corresponds to solid-state structure of the experimentally observed compound **3a** (compare Figure 1). It shows a planar, four-coordinate Pd(II) ion with monodentate ligands in trans arrangement. The ligands again use the lone pair of the nitrogen atom remote from the s-cis standing carbonyl group for complexation and are orientated in opposite directions (dipole moment = 0 D). The complexation energy for the formation of **6a** from **5a** and **4** is calculated to 35.7 kcal/mol (not including BSSE), a little less than for the complexation of **4**. The calculated geometrical parameters of the model structure **6a** (without substituents) agree with the observed X-ray structure of **3a** (e.g., Pd−N: calc. 2.072 Å, X-ray 2.035 Å, Pd−Cl 2.377 Å, X-ray 2.305 Å, see the Supporting Information).

Structure **6b** shows similar coordination, but parallel orientation of the ligands, with a higher relative energy of 1.15 kcal/mol. Other coordination sites and/or different orientations of the ligands lead also to higher relative energies, as expected from the 1:1 complexes (Figure 2).

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TABLE 1. Suzuki Cross-Coupling of Bromobenzene, Phenylboronic Acid, and Catalyst 3a under Various Reaction Conditions[a]

entry	catalyst concentration (mol %)	base	*T* (°C)	*t* (h)	yield (%)	TON
1	0.4	K_2CO_3	85	1	>99	250
2	0.5	K_2CO_3	50	48	86	172
3	0.1	K_2CO_3	85	3	87	870
4	0.1	K_2CO_3	85	24	92	920
5	0.01	K_2CO_3	85	72	41	4100
6	0.01	Cs_2CO_3	85	48	35	3500
7	0.01	K_2CO_3	110	24	94	9400
8	0.0017	K_2CO_3	110	4	97	58 000
9	4.5×10^{-4}	K_2CO_3	110	3	98	218 000

[a] Reaction conditions: PhBr (1 equiv), $PhB(OH)_2$ (1.2 equiv), base (2 equiv), **3a**, toluene.

However, these other arrangements are close in energy and it is difficult to discuss the influence of conformations in detail. Quite clearly cis structures such as **6k**,**m** are much higher in energy, especially when coordinated to oxygen (**6m**). In some examples, short distances (smaller than 2.3 Å) between chlorides and NH-protons (**6f**,**j**) or between NH and carbonyl oxygen atoms (2.19 Å, **6k**) are observed, but these interactions seem not to have predominant influences on the relative energies of the species.

Catalysis

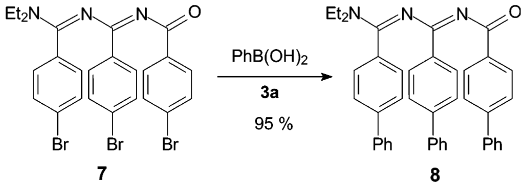
Palladium(II) complexes have great potential for the generation of catalytically active species, which have found many applications in synthetically useful reactions.[16,17] With regard to other palladium(II) complexes[18−20] with two-coordinate nitrogen atoms as ligands sites we have investigated the catalytic potential of the *N*-acylamidine complexes **3** in carbon−carbon cross-coupling reactions.

We focused our interest initially on Suzuki−Miyaura cross-coupling reactions,[21,22] which are particularly useful in organic synthesis because of comparatively mild reaction conditions and wide tolerance with respect to functional groups present.

Complex **3a** exerts high catalytic activity on the standard Suzuki−Miyaura system (1 equiv of bromobenzene and 1.2 equiv of phenylboronic acid) (Table 1) and proved to be an exceptionally good catalyst. Almost quantitative yields of biphenyl are produced at 110 °C with turnover numbers (TON) of 200 000 and more. In our experiments, potassium carbonate is a suitable base, similar to the more expensive cesium carbonate. Potassium carbonate as base and toluene as solvent at 110 °C lead to increasing yields with decreasing amounts of catalyst, possibly due to better turn over in more concentrated solutions (entries 7−9). These reactions are also very fast. For entry 9, a turnover frequency (TOF) of 206 000/h was determined, a quite large number for coupling of nonactivated aryl bromides with phenylboronic acid in comparison to published data.[23,24] Interestingly, complex **3a** is only sparingly soluble in cold toluene, which is probably an advantage during the initial steps toward the generation of the catalytically active species. Qualitatively, Pd(II) complexes of ligands **3b**,**c** show similar catalytic activity. For catalytic purposes, it is not necessary to separate and purify (crystallize) the complexes **3**. Addition of $PdCl_2(PhCN)_2$ to a solution of the *N*-acylamidine, stirring for a few hours and subsequent addition of the reaction partners leads to the cross-coupling products in similar yields as from the isolated crystalline complexes.

Chlorobenzene was also coupled to phenylboronic acid in the presence of 0.5% of **3a**, but the yield of biphenyl was significantly lower (ca. 20%) under the reaction conditions employed.

As a first example of the application of catalyst **3a** in synthesis, the 1-oxa-3,5-diaza-2,4,6-tris(4-bromophenyl)-7-dimethylaminohexatriene (**7**), an oligonitrile derivative from our laboratory,[25,26] was converted into the corresponding biphenyl compound **8** by reaction with phenylboronic acid in 95% isolated yield in the presence of 0.5% **3a**.



Complex **3a** is also active in Heck-type reactions,[18,27] as studied in bromobenzene couplings to styrene yielding stilbene at various reaction conditions. However, its applications are limited, possibly by its insufficient thermal stability. Heck reactions usually require high reaction temperatures. At a temperature of 140 °C, a yield of 87% is obtained after 2 days if sodium acetate is used as base in dimethylacetamide as solvent.[28] Darkening of the reaction mixture and precipitation of Pd indicates decomposition of the catalyst under these conditions.

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Conclusion

N-Acylamidines **2**, easily prepared by acylation of the respective amidines **1**, form 2:1 complexes **3** with $PdCl_2$ with trans configuration, acting as monodentate ligands via the nitrogen atom remote from the carbonyl group. The structures of the complexes **3a**−**c** were obtained by X-ray crystallography. As studied by DFT calculations, many isomeric structures **6** with different conformations and configurations are associated with local minima on the energy hyperface within an energy range of 4 kcal/mol. The complexes **3** show extraordinary catalytic activity in Suzuki−Miyaura cross-coupling reactions, either as isolated crystals or prepared in situ without isolation.

Experimental Section

***N*-Acylamidines 2: General Procedure for the Acylation of *N*-Alkylamidines 1. Method A.** To the *N*-alkylamidine **1** (20.0 mmol) was added a surplus of 2 M sodium hydroxide solution (25 mL). The mixture was stirred and cooled to 0 °C. A solution of acyl chloride (19.0 mmol) in acetone (10 mL) was added dropwise to the reaction mixture using a dropping funnel. Then, the suspension was allowed to warm to 10 °C over the course of 1.5 h. The remaining solid was filtered off and washed with water (50 mL), and the solvent was removed in vacuo.

Method B. To the *N*-alkylamidine **1** (10.0 mmol) was added a surplus of 2 M sodium hydroxide solution (10 mL). The mixture was stirred and cooled to 0 °C. A solution of acyl chloride (9.5 mmol) in acetone (5 mL) was added dropwise to the reaction mixture using a dropping funnel. Then, the suspension was allowed to warm to 10 °C over the course of 1.5 h. The solution was extracted with chloroform (3 × 10 mL). The combined organic layers were dried with magnesium sulfate, and the solvent was removed in vacuo. The resulting oil was purified by distillation.

General Procedure for the Preparation of *N*-Acylamidine−Pd(II) Complexes. A 0.10 mmol portion of *N*-acylamidine **2** was treated at room temperature with 0.05 mmol of bis(benzonitrile)palladium(II) chloride dissolved in a small amount of dichloromethane or of chloroform. A clear, yellow solution was formed. After 30 min, diethyl ether (2 mL) was added to the stirred solution. Then, another 10 mL of diethyl ether was carefully added to form an upper layer. Within hours or days crystals of **3** were formed, which were collected and washed with diethyl ether.

Catalysis. Typical Experimental Procedure for the Suzuki Coupling of Aryl Bromides with Phenylboronic Acid. A 100-mL round-bottom flask was charged with bromobenzene (1.57 g, 10 mmol), phenylboronic acid (1.46 g, 12 mmol), potassium carbonate (2.76 g, 20 mmol), catalyst **3a** (0.7 mg, 0.001 mmol, 0.01 mol % Pd), and 50 mL of toluene. The reaction was stirred at 110 °C in air, and the reaction progress was analyzed by GC. When completed, the reaction mixture was poured into an excess of water and extracted with dichloromethane (3 × 25 mL). The organic extract was dried and evaporated to afford the crude product in a 94% yield (pure by ^{1}H NMR).

Typical Experimental Procedure for the Heck Arylation of Alkenes. A 100-mL round-bottom flask was charged with bromobenzene (0.79 g, 5 mmol), styrene (0.72 g, 7 mmol), anhydrous sodium acetate (0.49 g, 6 mmol), catalyst **3a** (69.8 mg, 0.1 mmol, 2.0 mol % Pd), and 50 mL of *N*,*N*-dimethylacetamide. The reaction was stirred at 140 °C in air, and the reaction progress was analyzed by GC. After 2 days, the reaction mixture was poured into an excess of water and extracted with dichloromethane (3 × 25 mL). The organic extract was dried and evaporated to afford the crude product in a 87% yield (pure by ^{1}H NMR).

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Supporting Information Available: Detailed experimental procedures, spectroscopic and crystallographic data, and details of quantum chemical calculations (GAUSSIAN 98 Archive Entries). This material is available free of charge via the Internet at http://pubs.acs.org.

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