Inorganic Chemistry

Article

pubs.acs.org/IC

A Palladium(II) Center Activates Nitrile Ligands toward 1,3-Dipolar Cycloaddition of Nitrones Substantially More than the Corresponding Platinum(II) Center

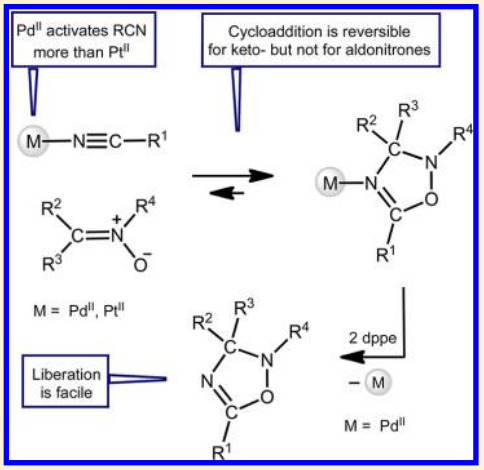
Andreii S. Kritchenkov,[†] Nadezhda A. Bokach,*[,†] Galina L. Starova,[†] and Vadim Yu. Kukushkin*[,†,‡]

[†]Department of Chemistry, St. Petersburg State University, Universitetsky Pr. 26, 198504 Stary Petergof, Russian Federation

[‡]Institute of Macromolecular Compounds of Russian Academy of Sciences, V.O. Bolshoii Pr. 31, 199004 St. Petersburg, Russian Federation

Supporting Information

ABSTRACT: Palladium(II)-coordinated NCR^1 (R^1 = Et (**1**), NMe_2 (**2**), Ph (**3**)) species react smoothly with acyclic nitrones such as the ketonitrones $Ph_2C{=}N(O)R^4$ (R^4 = *p*-MeC_6H_4 (**4**), *p*-ClC_6H_4 (**5**)) and the aldonitrone *p*-$MeC_6H_4CH{=}N(O)Me$ (**6**) in the corresponding nitrile media. This reaction proceeds as a consecutive two-step intermolecular cycloaddition to give the mono- and bis-2,3-dihydro-1,2,4-oxadiazole complexes $[PdCl_2(R^1CN)\{N^a{=}C(R^1)ON(R^4)C^b(R^2R^3)\}]^{(a-b)}$ (**7a−13a**; R^2, R^3 = Ph; R^4 = C_6H_4Me-*p*, R^1 = Et (**7**), NMe_2 (**8**), Ph (**9**); R^4 = C_6H_4Cl-*p*, R^1 = Et (**10**), NMe_2 (**11**), Ph (**12**); R^2 = H, R^3 = C_6H_4Me-*p*, R^4 = Me, R^1 = NMe_2 (**13**)) and $[PdCl_2\{N^a{=}C(R^1)ON(R^4)C^b(R^2R^3)\}_2]^{(a-b)}$ (**7b−13b**), respectively. Inspection of the obtained data and their comparison with the previous results indicate that the Pd^{II} centers provide substantially greater activation of RCN ligands toward the 1,3-dipolar cycloaddition than the relevant Pt^{II} centers. The palladium(II)-mediated 1,3-dipolar cycloaddition of ketonitrones to nitriles is reversible. All complexes were characterized by elemental analyses (C, H, N), high-resolution ESI-MS, and IR and ^{1}H and $^{13}C\{^1H\}$ NMR spectroscopy. The structure of *trans*-**7b** was determined by single-crystal X-ray diffraction. Metal-free 5-NR'_2-2,3-dihydro-1,2,4-oxadiazoles (**7c−13c**) were liberated from the corresponding (2,3-dihydro-1,2,4-oxadiazole)$_2Pd^{II}$ complexes by treatment with 1,2-(diphenylphosphino)ethane, and the heterocycles were characterized by high-resolution ESI^+-MS and ^{1}H and $^{13}C\{^1H\}$ spectroscopy.



INTRODUCTION

Nitriles exhibit a relatively high chemical inertness, but coordination of these species to a metal center dramatically enhances their reactivity in such a way that the reaction acceleration may reach a factor of 10^6−10^{10} and occasionally be even as high as 10^{18}.[1−3] The systematic experimental and theoretical studies on the reactivity of metal-bound nitriles toward nucleophiles, electrophiles, or, eventually, 1,3-dipoles in cycloadditions (CAs) demonstrated that the metal activation of RCN molecules opens up attractive routes for the generation of a great variety of compounds, i.e. iminoacylated O-, N-, and S-nucleophiles, carboxamides (including acrylamide and nicotinamide), azavinylidenes, tetrazoles, oxadiazoles, oxadiazolines, and cyanoolefins; many of these species are of significant basic, industrial, and/or pharmacological importance.[1−3]

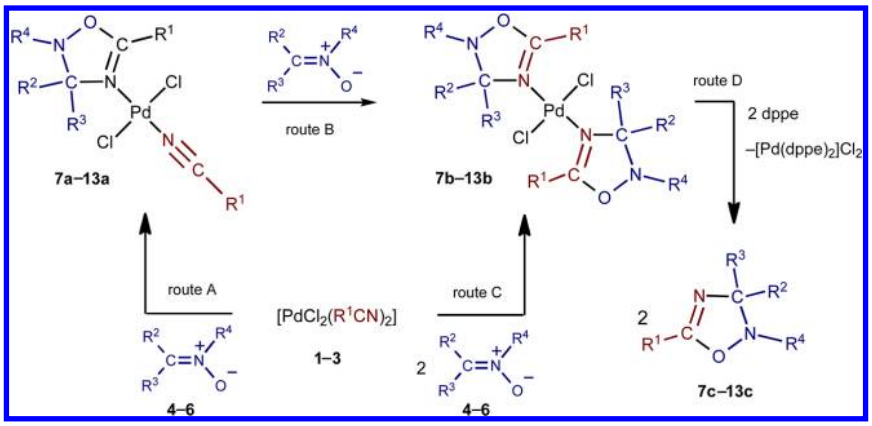
Currently a great amount of data regarding metal-mediated and metal-catalyzed cycloadditions to various organic substrates has been accumulated in the literature.[4] In particular, the activation of nitriles RCN, even unreactive species bearing the electron donor R, toward cycloadditions of allyl anion dipoles (e.g., nitrones[2c,5−7]) can be achieved by their ligation to a metal center. The nitrones are widely applied as 1,3-dipoles for both metal-free and metal-mediated generation of cyclic systems.[8] The nature and oxidation state of the metal centers play major roles in the control of the metal-mediated CA of nitrones. Thus, the 1,3-dipolar cycloaddition (DCA) proceeds easily under mild conditions only when nitriles are bound to platinum(II) or -(IV) and, in exceptional cases, to palladium(II) centers.[2c,5b,7c,9] However, the application of highly labile (nitrile)M^{IV} (M = Ti, Zr) complexes leads to the substitution of the nitrile ligands followed by some secondary processes.[9e]

On the basis of quantum chemical calculations[10] one can conclude that Pd^{II} centers—similarly to the relevant Pt^{II} centers—should also facilitate CAs. However, the greater kinetic lability of palladium(II) species and their higher hardness make the alternative reaction of nitrones, i.e. substitution of nitrile ligands with nitrones,[5b] quite probable. All these, in turn, significantly lower the selectivity of palladium(II)-mediated DCA, especially when the reaction is

Received: August 27, 2012

   dx.doi.org/10.1021/ic301866y | Inorg. Chem. XXXX, XXX, XXX−XXX

Scheme 1. Studied Cycloadditions



performed in non-nitrile solvents.[5b] Thus, the essential goal of this work was directed to provide insights into the reactivity of the palladium-bound nitriles in CA vs substitution.

In order to provide a greater control in palladium(II)-mediated DCA of nitrones to ligated nitriles and to direct the interplay of the reactants to the CA route, we suggested employing the following dipolarophile–dipole couples: (i) the so-called push–pull nitrile[5d] (Me_2NCN), and the conventional nitriles RCN (R = Et, Ph), as dipolarophiles and (ii) the aryl ketonitrones $Ph_2C{=}N(O)R^4$ as 1,3-dipoles. In general, the R_2NCN species are much better σ-donor ligands as compared to the conventional alkyl and aryl cyanides; the latter behave as only moderate net σ and π donors and are easily displaced by stronger ligands.[11] It is also important that dialkylcyanamide ligands are more reactive toward the DCA of nitrones than the alkylnitrile ligands.[5e] We were interested in a comparison of their reactivity and selectivity of DCA at palladium(II) centers. As dipoles, in addition to the aldonitrone, we addressed the little studied aryl ketonitrones, insofar as these dipoles are much more reactive in CA than the relevant aldonitrones conventionally used for studies of these reactions.[5e] Furthermore, we were interested in a comparison of their reactivity with RCN species at palladium(II) and platinum(II) metal centers.

Our goal was at least 4-fold: (i) to compare the effects of the nature of reactant(s) substituents for Pd^{II}-mediated DCA with those of the previously studied platinum(II)-based systems, (ii) to develop preparative experiments to compare the effect of the activation of nitrile ligands by Pd^{II} and Pt^{II} centers toward DCA of the nitrones, (iii) to develop a method of synthesis of 2,3-dihydro-1,2,4-oxadiazoles, consisting of metal-mediated DCA nitrones to nitriles followed by liberation of the heterocycle, and (iv) to study the possibility of a reversible Pd^{II}-mediated DCA.

RESULTS AND DISCUSSION

Palladium(II)-Mediated 1,3-Dipolar Cycloaddition. In the current work, the nitrile complexes $[PdCl_2(NCR^1)_2]$ (R^1 = Et (**1**), NMe_2 (**2**), Ph (**3**)) on one hand and the ketonitrones $Ph_2C{=}N(O)R^4$ (R^4 = *p*-MeC_6H_4 (**4**), *p*-ClC_6H_4 (**5**)) and the aldonitrone *p*-$MeC_6H_4CH{=}N(O)Me$ (**6**) on the other were employed as the reactants for the cycloaddition study (Scheme 1 and Table 1).

The reactions between **4**–**6** and the nitrile ligands R^1CN (R = Et, NMe_2, Ph) in their palladium(II) complexes (**1**–**3**), in all possible combinations, were performed in a solution of the corresponding nitrile, and they lead to the generation of 2,3-dihydro-1,2,4-oxadiazole complexes **7a**–**13a** and **7b**–**13b**. It should be pointed out that nitrones **4**–**6** do not react with uncomplexed nitriles R^1CN even under drastic conditions (240 h, reflux in the R^1CN media). The latter observation means that CA of the ketonitrones to the nitriles is Pd^{II}-mediated.

Table 1. Compound Numbering to Scheme 1

	$R^2/R^3/R^4$		
R^1	Ph/Ph/C_6H_4Me-*p* (**4**)	Ph/Ph/C_6H_4Cl-*p* (**5**)	H/C_6H_4Me-*p*/Me (**6**)
Et (**1**)	**7a–c**	**10a–c**	
NMe_2 (**2**)	**8a–c**	**11a–c**	**13a–c**
Ph (**3**)	**9a–c**	**12a–c**	

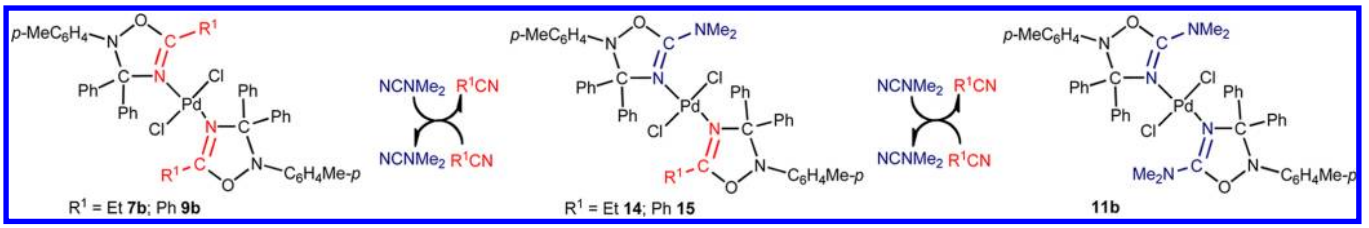
Although CA studied in this work is of general character, it proceed differently depending on (i) the nature of substituents in the R^1CN ligands, (ii) the nature of dipoles, viz., with the ketonitrones $Ph_2C{=}N(O)R^4$ or with the aldonitrone *p*-$MeC_6H_4C(H){=}N(O)Me$, and (iii) reaction conditions, such as the molar ratio of reactants and temperature. All these specific features are discussed in the following sections.

Reaction of Complexes 1–3 and Ketonitrones 4 or 5 in a 1:1 Molar Ratio. Ketonitrones **4** and **5** react with the nitrile R^1CN (R^1 = Et, Ph, NMe_2) ligand in **1**–**3** in a 1:1 molar ratio in a solution of the corresponding nitrile, and this reaction leads to mono-cycloadducts (mono-CAs) **7a**–**12a** (Scheme 1, route A).

Thus, the reaction between **4** or **5** and complex **3** in a 1:1 molar ratio in PhCN proceeds at room temperature for 30 min to give mono-CAs **9a** and **12a** in 88–90% yield. In contrast to the case for **3**, CA between **1** and **2** and ketonitrones **4** and **5** (in all possible combinations) in a 1:1 molar ratio at room temperature in EtCN or $NCNMe_2$, respectively, does not proceed selectively and brings about a broad mixture of products. Monitoring of this mixture by high-resolution ESI^+-MS allowed the identification of (i) mono-CAs **7a**, **8a**, **10a**, and **11a** (see the Experimental Section), (ii) Ph_2CO (*m*/*z* 107.0495 ($[M + H]^+$, calcd 107.0491), and (iii) $[PdCl_2\{ON(R^4){=}CPh_2\}_2]$ (R^4 = C_6H_4Me-*p*, *m*/*z* 431.0123 $[M - Cl]^+$, calcd 431.0127; R^4 = C_6H_4Cl-*p*, *m*/*z* 450.9583 $[M - Cl]^+$, calcd 450.9581). Benzophenone is apparently formed via a gradual Pd^{II}-mediated degradation of the ketonitrones, while the nitrone complex $[PdCl_2\{ON(R^4){=}CPh_2\}_2]$ originates from the substitution of the nitrile ligands in their palladium(II) complexes **1** and **2** with the ketonitrones; although *ketonitrones*

dx.doi.org/10.1021/ic301866y | Inorg. Chem. XXXX, XXX, XXX–XXX

Scheme 2. Nitrile Exchange in 7b (or 9b) via Retrocycloaddition



bound to Pd^{II} centers are unknown, Pd^{II} species bearing similar O-coordinated *aldonitrones* have been previously described.[5b]

A decrease of the reaction temperature to −20 °C allowed the selective generation of **7a**, **8a**, **10a**, and **11a** from **1** (or **2**) and **4** (or **5**) (molar ratio 1:1.3, in a solution of the corresponding nitrile), and these species were isolated in good yields (ca. 70% after recrystallization). Substitution of the nitrile ligands by the ketonitrones under these conditions was not observed.

We also conducted a comparative study of the reactivity of the complexes *trans*-$[MCl_2(R^1CN)_2]$ (M = Pd, Pt) in the reaction with the nitrones. Thus, the reaction between *trans*-$[MCl_2(PhCN)_2]$ and ketonitrones **4** or **5** (molar ratio 1:1, room temperature, in PhCN) is complete in 0.5 h (M = Pd) and does not proceed at all (M = Pt). The reaction between *trans*-$[MCl_2(R^1CN)_2]$ (R^1 = Et, NMe_2) and ketonitrones **4** and **5** (molar ratio 1:1 in R^1CN or in $CHCl_3$[5e]) is complete in 4 h (R^1 = NMe_2) and 6 h (R^1 = Et) at −20 °C (M = Pd) or at room temperature when M = Pt. All observations indicate the higher degree of activation of nitrile ligands toward DCA of ketonitrones by the Pd^{II} as compared to the Pt^{II} center.

Reaction of Complexes 1−3 with Ketonitrones 4 and 5 in a 1:2 Molar Ratio. When the molar ratio between palladium complexes **1**−**3** and the ketonitrones is 1:2, the reaction leads to bis-cycloadducts (bis-CAs) **7b**−**12b** (Scheme 1, route C). This interaction is a consecutive two-step cycloaddition (Scheme 1, routes A and B). Indeed, the treatment of 1 equiv of **7a**−**12a** with 1 equiv of **4** (or **5**) in the corresponding nitrile solution leads to selective generation of **7b**−**12b**.

The interaction of complex **3** and ketonitrones **4** or **5** and in a 1:2 molar ratio in PhCN proceeds at room temperature for 1 h to furnish bis-CAs **9b** and **12b**, isolated in 88−92% yields. The reaction between complexes **1** and **2** and ketonitrones **4** and **5** in the neat nitriles EtCN and $NCNMe_2$, respectively, in a 1:2 molar ratio is complete in ca. 4 h at room temperature to give yellow precipitates of **7b**, **8b**, **10b**, and **11b** in rather high yields (ca. 80−90%).

Reaction of Complex 2 with Aldonitrone 6. Although the Pd^{II}-mediated DCA of aldonitrones to the conventional (alkyl and aryl) nitrile ligands is known,[5b,9e] the palladium(II)-mediated CA of aldonitrones to the so-called push−pull nitrile ligands (e.g., dialkylcyanamides) has not yet been investigated. Our previous studies[5d] demonstrated that the platinum(II) center efficiently activates dialkylcyanamide ligands toward DCA of aldonitrones. Taking this into account, we attempted the reaction between aldonitrone **6** and *trans*-$[PdCl_2(NCNMe_2)_2]$ (**2**). The reaction of **2** and **6** in $NCNMe_2$ at room temperature is complete in 12 h to give mono-CA **13a** (molar ratio 1:1, Scheme 1, route A), and in 36 h to give bis-CA **13b** (molar ratio 1:2, Scheme 1, route B).

The previous studies demonstrated that an acetonitrile ligand in $[PdCl_2(MeCN)_2]$ reacts with aldonitrone **6** under more drastic conditions (reflux in MeCN, 1 day) as compared to those for a $NCNMe_2$ ligand in **2** and furnishes the bis-CA in moderate yields (10−20%).[5b] This difference indicates a higher dipolarophilicity of dialkylcyanamide ligands as compared to a conventional nitrile such as MeCN toward aldonitrones, and this observation is also in agreement with the data described earlier for Pt^{II}-mediated DCA.[5d] In addition, dialkylcyanamides are stronger σ donors than nitriles (Pickett parameter(s) for $NCNR_2$ range from −0.23 to −0.58 and for NCMe is −0.85[11]), which disfavors the substitution with aldonitrones and makes DCA to the nitrile functionality more selective for $NCNMe_2$ than for the poorer donor MeCN or EtCN ligands.

The DCA between *trans*-$[MCl_2(R^1CN)_2]$ (R^1 = Me, Et) and aldonitrone **6** (molar ratio 1:2 in R^1CN) is complete in 1 day under reflux (M = Pd) or does not proceed at all (M = Pt; 1 day, reflux). Moreover, we found that the reaction of *trans*-$[MCl_2(NCNMe_2)_2]$ and aldonitrone **6** (molar ratio 1:1, room temperature, in $NCNMe_2$) is complete in 12 h (M = Pd) or in 30 h (M = Pt). These synthetic experiments again indicate the higher degree of activation of nitriles toward DCA of aldonitrones by Pd^{II} as compared to the corresponding Pt^{II} center.

Reversibility of DCA. The completeness and the selectivity of DCA depend on the solubility of CA products. Thus, formation of poorly soluble bis-CAs occurs selectively with a high degree of conversion, while generation of soluble mono-CAs is accompanied by side reactions. These experimental observations give collateral evidence favoring the reversibility of DCA, and they agree well with our previous findings of the reversibility of platinum(II)-mediated DCA.[5e]

To obtain data additionally supporting the reversibility, we performed the following experiments. Complex **7b** (or **9b**) was stirred in $NCNMe_2$ solution for 2 days at room temperature, and the progress of the transformation (Scheme 2) was monitored by TLC. After disappearance of starting complex **7b** (or **9b**), compound **14** (or **15**) was isolated by column chromatography on SiO_2 (eluent $CHCl_3/Me_2CO$ 40/1 v/v). The total conversion of **7b** or **9b** into **11b** can be achieved in ca. 120 h. The reverse exchange also takes place, and **11b** was completely converted into **7b** by keeping the former in neat EtCN at room temperature for 7 days.

We also conducted an experiment indicating that the reversibility of DCA is specific for the metal-bound CA species **7b** and **9b** derived from ketonitrones **4** and **5**. Prolonged (100 h) stirring of **13b** (derived from aldonitrone **6**) in $NCNEt_2$ or in EtCN and PhCN at 35 °C gave no evidence for the appearance of other heterocycle-containing complexes in the mixture, and the starting materials remain intact. This observation can be rationalized by the higher thermodynamic stability of palladium(II)-bound 3-aryl-2,3-dihydro-1,2,4-oxadiazoles as compared to the ligated 3,3-*di*aryl-2,3-dihydro-1,2,4-oxadiazoles, due to the absence of steric repulsions between the phenyl groups and the metal fragment.

dx.doi.org/10.1021/ic301866y | *Inorg. Chem.* XXXX, XXX, XXX−XXX

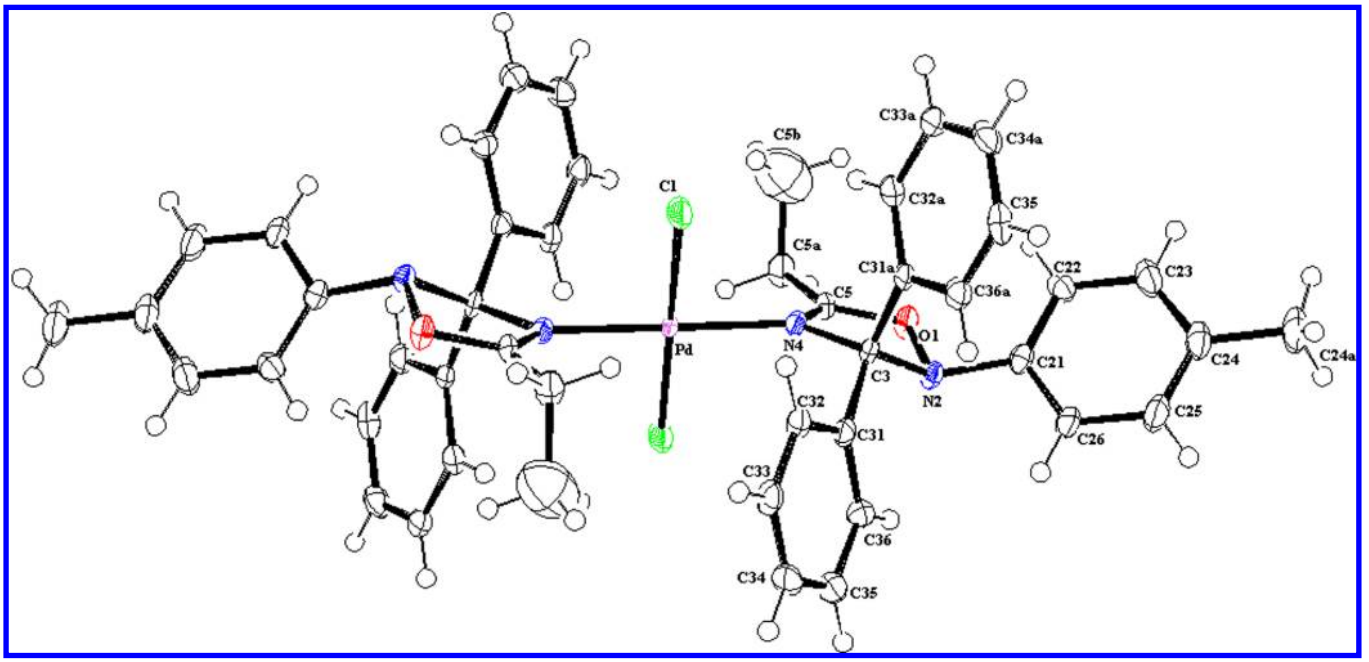


Figure 1. Thermal ellipsoid view of **7b** with the atomic numbering scheme. Thermal ellipsoids are drawn with 50% probability.

In previous work,[5e] we found the first example of the metal-mediated reversible CA of *C,C,N*-triaryl ketonitrones to nitrile ligands, observed at Pt^{II} centers. Herein we have demonstrated that the palladium(II)-mediated DCA of the ketonitrones to nitriles can be reversible; therefore, the reversibility of metal-mediated CA of ketonitrones to nitriles has more general character.

Liberation of the Heterocyclic Ligands. Several methods for the liberation of various nitrogen heterocycles from their palladium(II) complexes have been developed, and they are based on displacement with diphosphines,[5b,7b,12] excess Na_2S,[5b] or methylamine.[9e] Earlier we performed the synthesis of the 3-dialkylamino-2,3-dihydro-1,2,4-oxadiazoles and 3,3-diaryl-2,3-dihydro-1,2,4-oxadiazoles that is based on platinum-mediated CA followed by the liberation of the newly formed heterocyclic ligands. It appears that the ligands are so strongly bound to the platinum(II) center that their decoordination was achieved only by the treatment of the platinum complexes with an excess of a powerful ligand such as CN^-, conducted in accord with the Leung method.[5d,e,13]

In contrast to the kinetically inert platinum(II) species, the relevant palladium(II) complexes are logically[5b,9e,14] much more labile, and in accord with our expectations, we observed that the decoordination does not require a strong ligand such as CN^- and it can be achieved with 1,2-(diphenylphosphino)-ethane (dppe). Indeed, the treatment of **7b**−**13b** with 2 equiv of dppe for 4 h at room temperature (Scheme 1, route D) leads to almost quantitative formation of uncomplexed heterocycles **7c**−**13c** in solution along with a colorless precipitate of the well-known $[Pd(dppe)_2](Cl)_2$.[15] Hence, palladium(II)-based generation of 2,3-dihydro-1,2,4-oxadiazoles is much more synthetically favorable in comparison to the approach based on application of the appropriate platinum(II) species. First, the palladium(II) center activates the nitrile ligands more strongly than the Pt^{II} center, and second, the liberation of 2,3-dihydro-1,2,4-oxadiazoles could be achieved easily and conducted under mild conditions.

Characterization of 7a−13a and 7b−13b. Complexes **7a**−**13a** and **7b**−**13b** were obtained as yellow solids and characterized by elemental analyses (C, H, N), high-resolution ESI^+-MS, IR and and ^1H and $^{13}C\{^1H\}$ NMR spectroscopy and also by X-ray diffraction (**7b**). All palladium species gave satisfactory microanalyses. In the ESI^+-MS, the typical ions that were detected are $[M + H]^+$, $[M + Na]^+$, and $[M + K]^+$. A comparison of the IR spectra of the products with those of starting **1**−**3** indicated the absence of $\nu(C{\equiv}N)$ stretching vibrations at ca. 2300 cm^{-1} for **7b**−**13b**, while for **7a**−**13a** these stretches are displayed in the expected region from 2290 to 2310 cm^{-1}. The presence of intense $\nu(C{=}N)$ vibrations in the range between 1630 and 1667 cm^{-1} was detected in the IR spectra of all complexes.

For **7a**−**13a** and **7b**−**13b** signal integrations in the ^1H NMR spectra give evidence that the reaction between each of the coordinated nitriles and the nitrone proceeds in a 1:1 ratio. Both ^1H and $^{13}C\{^1H\}$ NMR spectra of **7a**−**13a** exhibit signals from the 2,3-dihydro-1,2,4-oxadiazole and the nitrile ligands. The ^1H NMR spectra of **8a**, **11a**, and **13a** display broad (owing to hindered rotation around the $C^3{-}NMe_2$ bond) singlets of the CH_3 protons from $C^3{-}NMe_2$ (3.63−3.78 ppm). The less broad signals from these protons of bis-CA species are shifted to low field by 0.53−0.69 ppm, relative to the corresponding signals from mono-CAs. In the ^1H NMR spectra of **7a**, **10a** and **7b**, **10b**, the quartets due to the CH_2 protons from the $C^3{-}Et$ atom appeared in almost the same range as for mono- and bis-CA species. In the $^{13}C\{^1H\}$ NMR spectra, peaks due to $C^5{=}N$ (158.4−166.8 ppm) and C^3 (98.1−98.6 ppm) were recognized.

Complex **7b** was additionally characterized by single-crystal X-ray diffraction (Figure 1). In **7b**, the coordination polyhedron of the Pd atom is a slightly distorted square plane with the heterocyclic ligands in trans positions. The Pd−N(4) bond (2.038(3) Å) is typical for (imine)Pd^{II} species,[16] while the Pd−Cl bond (2.2851(11) Å) is specific for palladium(II) chlorides.[16] The N(4)−C(5) distance (1.252(5) Å) is characteristic for a N=C double bond,[16] while the N(4)−C(3) (1.508(4) Å) and the N(2)−C(3) distances (1.523(5) Å)

dx.doi.org/10.1021/ic301866y | *Inorg. Chem.* XXXX, XXX, XXX−XXX

are specific for a typical N−C single bond, and all these distances are close to related bond lengths in the previously reported[5e] (2,3-dihydro-1,2,4-oxadiazole)$_2$Pt^{II} complex (N(4)−C(5) = 1.283(3)Å, N(4)−C(3) = 1.492(3)Å, N(2)−C(3) = 1.519(3) Å). In the crystal structure of **7b**, pseudolayers of {Cl_2Pt} and fragments of the organic ligand (parallel to plane *yz*) were found (Figure S1, Supporting Information). The Cl atoms interact with the neighboring molecules via C−H···Cl contacts; one of them is a rather strong bond, and the other one forms the hydrogen bridge (Table S1 and Figure S2, Supporting Information).

Characterization of 14 and 15. Complexes **14** and **15** were obtained as yellow solids and characterized by elemental analyses (C, H, N), high-resolution ESI$^+$-MS, and IR and ^{1}H and ^{13}C{^{1}H} NMR spectroscopy. All palladium species gave satisfactory microanalyses. In the high-resolution ESI$^+$-MS, the typical ions [M + Na]$^+$ were detected. The presence of intense ν(C═N) vibrations at 1658 (**14**) and 1651 cm^{-1} (**15**) was detected in the IR spectra of the complexes. The ^{1}H NMR spectra of **14** and **15** display broad (owing to hindered rotation around the C^3−NMe_2 bond) singlets of the CH_3 protons from C^3−NMe_2 (3.06−3.08 ppm). In the ^{1}H NMR spectra of **14**, the quartet due to the CH_2 protons from C^3−Et was detected. In the ^{13}C{^{1}H} NMR spectra, peaks due to C^5═N (161.0−162.3) and C^3 (98.3−98.5 ppm) were recognized.

Characterization of 9c−12c. Although **7c**, **8c**, and **13c** are known and their preparation and characterization has been described recently by us,[5d,e] the new metal-free 2,3-dihydro-1,2,4-oxadiazole species **9c−12c** were characterized by high-resolution ESI$^+$ mass spectrometry and ^{1}H and ^{13}C{^{1}H} NMR spectroscopy. In the ESI$^+$-MS, the observed peaks were attributed to [M + H]$^+$ and [M + Na]$^+$. ^{13}C{^{1}H} NMR spectra of the 2,3-dihydro-1,2,4-oxadiazoles demonstrate all signals specific for these heterocycles; the liberated species exhibit characteristic signals from C^{3a} (96.3−97.5 ppm) and C═N (161.2−162.0 ppm).

FINAL REMARKS

The results obtained in this work could be considered from a few perspectives. First, for palladium(II)-mediated DCA, we observed the same effects of the nature of reactant(s) substituents as in the previously studied platinum(II)-based systems.[2c,5e] Thus, PhCN and R_2NCN species are more reactive in CA than AlkCN complexes. Furthermore, the ketonitrones are more reactive in DCA as compared to the corresponding aldonitrones. All these findings together point out that the switch of platinum[2c,5e] to palladium (this work) does not affect the type of CA in Sustman's classification.[17] At both metal centers it belongs to the normal electron demand DCA, when the outcome of the reaction is determined by the $HOMO_{dipole}$−$LUMO_{dipolarophile}$ gap.

Second, inspection of the data obtained for palladium(II) and previous results on the corresponding platinum(II)-based systems explicitly indicate that, under strictly similar conditions, Pd^{II} centers provide substantially higher activation of RCN ligands toward CA than the relevant Pt^{II} centers. Taking into account the significant increase of asynchronicity in CA of nitrones to ligated nitrile species as compared to CA of metal-free reactants,[14,18] the former type of cycloaddition resembles the nucleophilic addition to metal-activated nitriles. In this context, it is worth mentioning that a similar trend in reactivity upon alteration of metal centers was observed by Lippert and colleagues,[19] who studied the hydration of nitriles ligated to [M(en)$_2$]$^{2+}$ centers; the rate of the water addition found for M = Pd^{II} was substantially higher than for M = Pt^{II}. However, our experimental results along with literature data on metal-mediated DCA should be further interpreted theoretically and appropriate calculations are on the way in our group.

Third, the directing of the interplay of nitrones to either CA to nitrile ligands or a nitrile substitution route depends on a delicate balance between the donor/acceptor properties of substituents at both reactants, the activating power of the metal center toward DCA, and its substitution inertness/lability toward interaction with the reactants. From this perspective the Pd^{II} center occupies an intermediate position between substitutionally inert, strong RCN activators such as Pt^{II} and Pt^{IV} centers (where only selective cycloaddition of both nitrones and nitrile oxides[2c] was observed) and kinetically labile nitrile Ti^{IV} and Zr^{IV} systems (where only displacement of nitriles by nitrones was found).[9e]

Fourth, CA of the nitrones to the push−pull dialkylcyanamide systems proceeds differently as compared to CA with the conventional alkyl- and arylnitriles. Thus, in the case of R_2NCN ligands at palladium(II) (this work) and platinum(II)[5d,e] centers we always observed a higher selectivity of CA that might be associated with better σ-donor properties of these species as compared to RCN species[11] that make the side substitution reaction with nitrones less favorable.

Fifth, we developed a two-step procedure for the previously unknown 3,3-diaryl-2,3-dihydro-1,2,4-oxadiazoles via Pd^{II} (this work)- and Pt^{II}-mediated[5e] generation of the ligated heterocycles followed by the liberation of dihydrooxadiazole species by the displacement with 1,2-(diphenylphosphino)ethane (this work) or NaCN.[5e] The palladium(II)-based system has obvious advantages over the platinum system. Indeed, the Pd^{II} center provides a higher activation of RCN species and CA could be performed under milder conditions. Furthermore, the liberation of Pd^{II}-bound oxadiazoles is much easier as compared to that of the Pt^{II} systems. It is also important that the palladium(II)-based procedure is more cost efficient that the platinum method.

Further studies may be associated with the search for more labile and low-cost 3d metal systems for metal-mediated or, in the most advantageous case, metal-catalyzed DCA. In addition, we will attempt CA of less usual and rather inert dipoles, whose interplay with metal-free RCN species is yet unknown and even hardly possible.

EXPERIMENTAL SECTION

Materials and Instrumentation. Solvents were obtained from commercial sources and used as received. Complexes **1−3** were synthesized in accord with the published procedures.[20] Nitrones **4** and **5** were obtained in according with the previously described protocol[21] by the reaction of aryl nitroso compounds with diphenyldiazomethane in diethyl ether at room temperature (60−85%). Nitrone **6** was obtained by the condensation of *N*-methyl hydroxylamine with *p*-tolylaldehyde by the known method.[22] C, H, and N elemental analyses were carried out by the Department of Organic Chemistry of St. Petersburg State University on a Hewlett-Packard 185B Carbon Hydrogen Nitrogen Analyzer. Electrospray ionization mass spectra were obtained on a Bruker micrOTOF spectrometer equipped with an electrospray ionization (ESI) source. The instrument was operated in both positive and negative ion modes using a *m*/*z* range of 50−3000. The capillary voltage of the ion source was set at −4500 V (ESI$^+$-MS) and the capillary exit at ±(70−150) V. For ESI species were dissolved in MeCN; $NaBF_4$ or formic acid was used as addition ionization agent. In the isotopic pattern, the most intense peak is reported. TLC was performed on Merck 60 F_{254} SiO_2 plates. Infrared spectra (4000−400

dx.doi.org/10.1021/ic301866y | Inorg. Chem. XXXX, XXX, XXX−XXX

cm^{-1}) were recorded on a Shimadzu FTIR-8400S instrument as KBr pellets. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ on a Bruker DPX-300 spectrometer at ambient temperature.

X-ray Structure Determination. The XRD single-crystal experiment was conducted at the X-ray Diffraction Center of St. Petersburg State University. The X-ray diffraction data were collected on a Bruker Kappa Apex II DUO diffractometer using Mo Kα radiation (λ = 0.710 73 Å) at 100 K. APEX2[23] software packages were used for cell refinements and data reductions. The structures were solved by direct methods using the SIR-92[24] program with the WinGX[25] graphical user interface. A semiempirical absorption correction (SADABS)[26] was applied. Structural refinements were carried out using SHELXL-97.[27] The hydrogens were positioned geometrically and constrained to ride on their parent atoms, with C−H = 0.95−0.99 Å and U_{iso} = 1.2−1.5U_{eq} (parent atom) (Table S2, Supporting Information).

Synthetic Work. *Reaction of Complexes 1−3 with Nitrones 4−6 in a 1:1 Molar Ratio.* A solution of **4** or **5** (0.1 mmol) in the corresponding nitrile R^1CN (R^1 = Et, NMe_2, Ph; 1 mL) was added to a solution of $[PdCl_2(R^1CN)_2]$ (**1−3**: 0.13 mmol, R^1 = Et; 0.01 mmol, R^1 = Ph, NMe_2) in R^1CN (1 mL). The reaction mixture was stirred at −20 °C (R^1 = Et, NMe_2) or room temperature (R^1 = Ph) for 30 min (R^1 = Ph), 4 h (R^1 = NMe_2), or 6 h (R^1 = Et). In the cases of R^1 = Et, NMe_2, the solvent was evaporated in vacuo at room temperature to give oily residues. Complexes **7a** and **10a** were purified by recrystallization from $CHCl_3$/*n*-hexane (4/1 v/v), while the yellow residues of **8a** and **11a** were crystallized under a layer of *n*-hexane at room temperature and washed with three 5 mL portions of a *n*-hexane/Et_2O mixture (4/1 v/v). For R^1 = Ph, 10 mL of *n*-hexane was added at the end of the reaction, whereupon the yellow precipitates of **9a** and **12a** were separated by filtration. The yellow powders of **7a−12a** were dried in air at room temperature. Yields: 69−88%.

A solution of the nitrone *p*-$MeC_6H_4CH{=}N(O)Me$ (0.1 mmol) in $NCNMe_2$ (1 mL) was added to a solution of $[PdCl_2(NCNMe_2)_2]$ (0.1 mmol) in $NCNMe_2$ (1 mL). The reaction mixture was stirred at room temperature for 12 h. The solvent was evaporated in vacuo at 25 °C to give the oily residue of **13a**. The residue was crystallized under a layer of *n*-hexane and washed with *n*-hexane/Et_2O, (4/1 v/v, three 5 mL portions) and dried in air at room temperature. Yield: 92%.

Reaction of Complexes 1−3 with Nitrones 4−6 in a 1:2 Molar Ratio. A solution of ketonitrone **4** or **5** (0.2 mmol) in the corresponding nitrile R^1CN (R^1 = Et, Ph, NMe_2; 1 mL) was added to a solution of $[PdCl_2(R^1CN)_2]$ (0.1 mmol) in R^1CN (1 mL). The reaction mixture was stirred at room temperature for 4 h (R^1 = Et, NMe_2) or for 1 h (R^1 = Ph). For R^1 = Et, NMe_2 the yellow precipitates of **7b**, **8b**, **10b**, and **11b** were separated by filtration and washed with *n*-hexane (three 1 mL portions). For R^1 = Ph *n*-hexane (10 mL) was added at the end of the reaction, whereupon the yellow precipitate of **9b** or **12b** was filtered off. The yellow powders of **7b−12b** were dried in air at room temperature. Yields: 88−92%.

A solution of the nitrone *p*-$MeC_6H_4CH{=}N(O)Me$ (0.2 mmol) in $NCNMe_2$ (1 mL) was added to a solution of $[PdCl_2(NCNMe_2)_2]$ (0.1 mmol) in $NCNMe_2$ (1 mL). The reaction mixture was stirred at room temperature for 36 h. The solvent was evaporated in vacuo at room temperature to give an oily residue of **13b**. The residue was crystallized from *n*-hexane and washed with *n*-hexane/Et_2O (4/1 v/v; three 5 mL portions) and dried in air at room temperature. Yield: 91%.

Characterization of Mono-CA Species. **7a**: 40.1 mg, 70%. Anal. Found: C, 44.38; H, 4.71; N, 7.33. Calcd for $C_{26}H_{27}N_3Cl_2OPd$: C, 44.32; H, 4.73; N, 7.31). High-resolution ESI$^+$: *m*/*z* 599.0666 ([M + Na]$^+$ requires 599.0558). The complex decomposes on SiO_2, and this prevented TLC monitoring. IR ν_{max}/cm^{-1} (KBr): 2934 m (C−H), 1637 s (C=N). δ_H (300 MHz, $CDCl_3$): 1.29 (3H, t, *J* = 7.6 Hz, CH_3 from Et of the 2,3-dihydro-1,2,4-oxadiazole ligand), 1.57 (3H, s, CH_3 from Et of the nitrile ligand), 2.14 (3H, s, CH_3 from C_6H_4Me-*p*), 2.19 (2H, s, CH_2 from Et of the nitrile ligand), 2.81 (2H, q, *J* = 7.6 Hz, CH_2 from Et of the 2,3-dihydro-1,2,4-oxadiazole ligand), 6.46 (2H, d, *o*-protons from C_6H_4Me-*p*), 6.70 (2H, d, *m*-protons from C_6H_4Me-*p*), 7.27 and 7.50 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 9.9 and 10.3 (CH_3 from Et of the nitrile and the 2,3-dihydro-1,2,4-oxadiazole ligand), 13.1 (CH_2 from Et of the nitrile ligand), 21.2 (CH_3 from C_6H_4Me-*p*), 23.2 (CH_2 from Et of the 2,3-dihydro-1,2,4-oxadiazole ligand), 98.4 (N−C−N), 121.0, 124.8, 127.5, 129.0, 129.5, 131.5, 135.0, and 141.1 ($C_{aromatic}$), 162.2 (C(O)=N); the C≡N carbon was not detected.

8a: 51.1 mg, 85%. Anal. Found: C, 51.62; H, 4.84; N, 11.58. Calcd for $C_{26}H_{29}N_5Cl_2OPd$: C, 51.63; H, 4.83; N, 11.58). High-resolution ESI$^+$: *m*/*z* 607.0958 ([M + H]$^+$ requires 607.0956). The complex decomposes on SiO_2, and this prevented TLC monitoring. IR ν_{max}/cm^{-1} (KBr): 2930 m (C−H), 2310 s (C≡N), 1667 s (C=N). δ_H (300 MHz, $CDCl_3$): 2.22 (3H, s, CH_3 from C_6H_4Me-*p*), 2.86 (6H, s, NMe_2 of the nitrile ligand), 3.75 (6H, br s, NMe_2 of the 2,3-dihydro-1,2,4-oxadiazole ligand), 6.57 (2H, d, *o*-protons from C_6H_4Me-*p*), 6.83 (2H, d, *m*-protons from C_6H_4Me-*p*), 7.29, and 7.46 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 21.6 (CH_3 from C_6H_4Me-*p*), 40.4, 40.6 (NMe_2 of the 2,3-dihydro-1,2,4-oxadiazole ligand and of the nitrile ligand), 98.5 (N−C−N), 121.5, 126.8, 128.1, 129.6, 132.7, 136.1, 138.2, and 141.7 ($C_{aromatic}$), 161.3 (C(O)=N); the C≡N carbon was not detected.

9a: 58.9 mg, 88%. Anal. Found: C, 60.90; H, 4.09; N, 6.25. Calcd for $C_{34}H_{27}N_3Cl_2OPd$: C, 60.87; H, 4.06; N, 6.26. High-resolution ESI$^+$: *m*/*z* 672.0662 ([M + Na]$^+$ requires 672.0660). The complex decomposes on SiO_2, and this prevented TLC monitoring. IR ν_{max}/cm^{-1} (KBr): 2933 m (C−H), 1630 s (C=N). δ_H (300 MHz, $CDCl_3$): 2.40 (3H, t, CH_3 from *p*-tol), 7.19, 7.41, 7.56, 7.69, 7.72, 7.81 (24H, 6 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 10.0 (CH_3 from *p*-tol), 98.2 (N−C−N), 121.0, 124.6, 127.4, 129.0, 129.5, 131.6, 132.3, 133.1, 135.0, and 141.0 ($C_{aromatic}$), 162.0 (C(O)=N); the C≡N carbon was not detected.

10a: 40.9 mg, 69%. Anal. Found: C, 50,45; H, 4.08; N, 7.04. Calcd for $C_{25}H_{24}N_3Cl_3OPd$: C, 50.44; H, 4.06; N, 7.06. High-resolution ESI$^+$: *m*/*z* 619.0011 ([M + Na]$^+$ requires 619.0012). The complex decomposes on SiO_2, and this prevented TLC monitoring. IR ν_{max}/cm^{-1} (KBr): 2936 m (C−H), 1636 s (C=N). δ_H (300 MHz, $CDCl_3$): 1.30 (3H, t, *J* = 7.6 Hz, CH_3 from Et of the 2,3-dihydro-1,2,4-oxadiazole ligand), 1.57 (3H, s, CH_3 from Et of the nitrile ligand), 2.19 (2H, s, CH_2 from Et of the nitrile ligand), 2.82 (2H, q, *J* = 7.6 Hz, CH_2 from Et of the 2,3-dihydro-1,2,4-oxadiazole ligand) 6.49 (2H, d, *o*-protons from C_6H_4Cl-*p*), 6.88 (2H, d, *m*-protons from C_6H_4Cl-*p*), 7.32 and 7.50 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 9.9 and 10.3 (CH_3 from Et of the nitrile and the 2,3-dihydro-1,2,4-oxadiazole ligand), 13.1 (CH_2 from Et of the nitrile ligand), 22.9 (CH_2 from Et of the 2,3-dihydro-1,2,4-oxadiazole ligand), 98.3 (N−C−N), 122.8, 127.3, 126.9, 128.5, 129.2, 132.0, 137.7, and 143.1 ($C_{aromatic}$), 159.7 (C(O)=N); the C≡N carbon was not detected.

11a: 54.2 mg, 87%. Anal. Found: C, 48.04; H, 4.19; N, 11.19. Calcd for $C_{25}H_{26}N_5Cl_3OPd$: C, 48.02; H, 4.19; N, 11.20. High-resolution ESI$^+$: *m*/*z* 649.0293 ([M + Na]$^+$ requires 649.0297). The complex decomposes on SiO_2, and this prevented TLC monitoring. IR ν_{max}/cm^{-1} (KBr): 2931 m (C−H), 2290 m (C≡N), 1664 s (C=N). δ_H (300 MHz, $CDCl_3$): 2.85 (6H, s, NMe_2 of the nitrile ligand), 3.78 (6H, br s, NMe_2 of the 2,3-dihydro-1,2,4-oxadiazole ligand), 6.69 (2H, d, *o*-protons from C_6H_4Cl-*p*), 7.03 (2H, d, *m*-protons from C_6H_4Cl-*p*), 7.35, and 7.62 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 40.4, 40.6 (NMe_2 of the 2,3-dihydro-1,2,4-oxadiazole ligand and of the nitrile ligand), 98.4 (N−C−N), 122.3, 127.3, 128.4, 129.3, 131.2, 131.8, 137.3, and 143.0 ($C_{aromatic}$), 161.3 (C(O)=N); the C≡N carbon was not detected.

12a: 56.7 mg, 82%. Anal. Found: C, 57.36; H, 3.49; N, 6.09. Calcd for $C_{33}H_{24}N_3Cl_3OPd$: C, 57.33; H, 3.50; N, 6.08. High-resolution ESI$^+$: *m*/*z* 715.0011 ([M + Na]$^+$ requires 715.0012). The complex decomposes on SiO_2, and this prevented TLC monitoring. IR ν_{max}/cm^{-1} (KBr): 2932 m (C−H), 1630 s (C=N). δ_H (300 MHz, $CDCl_3$): 7.18, 7.40, 7.56, 7.69, 7.70, 7.73, 7.80 (6 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 98.4 (N−C−N), 121.1, 124.6, 127.4, 129.1, 129.5, 131.5, 133.2, 135.2, and 141.0 ($C_{aromatic}$), 162.1 (C(O)=N); the C≡N carbon was not detected.

13a: 38.6 mg, 92%. Anal. Found: C, 37.21; H, 4.67; N, 15.47. Calcd for $C_{15}H_{23}N_5Cl_2OPd$: C, 37.15; H, 4.68; N, 15.47. High-resolution ESI$^+$: *m*/*z* 491.0303 ([M + Na]$^+$ requires 491.0306). The complex decomposes on SiO_2, and this prevented TLC monitoring. IR ν_{max}/

dx.doi.org/10.1021/ic301866y | Inorg. Chem. XXXX, XXX, XXX−XXX

cm^{-1} (KBr): 2931, m (C−H), 2291 m (C≡N), 1666 s (C═N). δ_H (300 MHz, $CDCl_3$): 2.31 (3H, s, CH_3 from C_6H_4Me-*p*), 2.91 (9H, br s, N(O)Me, NMe_2 of the nitrile ligand), 3.63 (6H, br s, NMe_2 of the 2,3-dihydro-1,2,4-oxadiazole ligand), 5.55 (1H, s, CH), 7.17 (2H, d, *m*-H from *p*-tol), 7.47 (2H, d, *o*-H from C_6H_4Me-*p*). δ_C (75.5 MHz, $CDCl_3$): 21.8 (CH_3 from *p*-tol), 40.3 (NMe_2 of the 2,3-dihydro-1,2,4-oxadiazole ligand), 40.4 (NMe_2 of the nitrile ligand), 46.2 (N(O)Me), 93.1 (N−C−N), 128.5, 129.4, 135.09, and 139.1 ($C_{aromatic}$), 158.4 (C(O)═N); the C≡N carbon was not detected.

Characterization of Bis-CA Species. **7b**: 78.2 mg, 90%. Anal. Found: 64.10; H, 5.12; N, 6.53. Calcd for $C_{46}H_{44}N_4Cl_2O_2Pd$: C, 64.08; H, 5.14; N, 6.50. High-resolution ESI$^+$: *m*/*z* 902.1607 ($[M + K]^+$ requires 902.1607). R_f = 0.39 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2934, 2978 m (C−H), 1643 s (C═N). δ_H (300 MHz, $CDCl_3$): 1.30 (3H, t, *J* = 7.6 Hz, CH_3 from Et), 2.14 (3H, s, CH_3 from C_6H_4Me-*p*), 2.81 (2H, q, *J* = 7.6 Hz, CH_2 from Et), 6.46 (2H, d, *o*-protons from C_6H_4Me-*p*), 6.70 (2H, d, *m*-protons from C_6H_4Me-*p*), 7.28, and 7.50 (10H, 2 m, $H_{aromatic}$). δ_C 10.0 (CH_3 from Et), 21.2 (CH_3 from C_6H_4Me-*p*), 22.6 (CH_2 from Et), 98.3 (N−C−N),122.1, 126.7, 128.6, 128.8, 132.8, 135.8, 138.2, and 141.3 ($C_{aromatic}$), 161.1 (C(O)═N).

8b: 78.3 mg, 88%. Anal. Found: C, 61.97; H, 5.20; N, 9.39. Calcd for $C_{46}H_{46}N_6Cl_2O_2Pd$: C, 61.92; H, 5.20; N, 9.42. High-resolution ESI$^+$: *m*/*z* 894.2264 ($[M + H]^+$ requires 894.2266). R_f = 0.40 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2933 m (C−H), 1648 s (C═N). δ_H (300 MHz, $CDCl_3$): 2.21 (3H, s, CH_3 from C_6H_4Me-*p*), 3.06 (6H, br s, NMe_2), 6.34 (2H, d, *o*-protons from C_6H_4Me-*p*), 6.77 (2H, d, *m*-protons from C_6H_4Me-*p*), 7.29, and 7.46 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 21.5 (CH_3 from C_6H_4Me-*p*), 39.9 (NMe_2), 98.5 (N−C−N), 122.3, 127.0, 128.4, 128.9, 132.3, 135.8, 138.1, and 141.8 ($C_{aromatic}$), 161.2 (C(O)═N).

9b: 75.5 mg, 79%. Anal. Found: C, 67.67; H, 4.66; N, 5.83. Calcd for $C_{54}H_{44}N_4Cl_2O_2Pd$: C, 67.68; H, 4.63; N, 5.85. High-resolution ESI$^+$: *m*/*z* 982.1864 ($[M + Na]^+$ requires 982.1868). R_f = 0.37 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2933 m (C−H), 1630 s (C═N). δ_H (300 MHz, $CDCl_3$): 2.40 (3H, t, CH_3 from *p*-tol), 7.20, 7.43, 7.55, 7.70, 7.82 (19H, 5 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 10.1 (CH_3 from *p*-tol), 98.3 (N−C−N), 121.1, 124.6, 127.5, 129.0, 129.5, 132.3, 133.2, 135.1, and 141.1 ($C_{aromatic}$), 162.2 (C(O)═N).

10b: 82.8 mg, 92%. Anal. Found: C, 58.50; H, 4.26; N, 6.21. Calcd for $C_{44}H_{38}N_4Cl_4O_2Pd$: C, 58.52; H, 4.24; N, 6.20. High-resolution ESI$^+$: *m*/*z* 926.0774 ($[M + Na]^+$ requires 0926.0776). R_f = 0.42 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2934 m (C−H), 1637 s (C═N). δ_H (300 MHz, $CDCl_3$): 1.30 (3H, t, *J* = 7.6 Hz, CH_3 from Et), 2.82 (2H, q, *J* = 7.6 Hz, CH_2 from Et), 6.49 (2H, d, *o*-protons from C_6H_4Cl-*p*), 6.88 (2H, d, *m*-protons from C_6H_4Cl-*p*), 7.32, and 7.50 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 9.9 (CH_3 from Et), 22.6 (CH_2 from Et), 98.4 (N−C−N), 123.3, 127.2, 128.3, 131.5, 132.7, 137.8, and 142.9 ($C_{aromatic}$), 160.1 (C(O)═N).

11b: 85.6 mg, 92%. Anal. Found: C, 56.60; H, 4.34; N, 9.02. Calcd for $C_{44}H_{40}N_6Cl_4O_2Pd$: C, 56.64; H, 4.32; N, 9.01. High-resolution ESI$^+$: *m*/*z* 934.1177 ($[M + H]^+$ requires 934.1177). R_f = 0.42 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2928 m (C−H), 1666 s (C═N). δ_H (300 MHz, $CDCl_3$): 3.05 (6H, br s, NMe_2), 6.40 (2H, d, *o*-protons from C_6H_4Cl-*p*), 6.94 (2H, d, *m*-protons from C_6H_4Cl-*p*), 7.29, and 7.43 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 39.9 (NMe_2), 98.6 (N−C−N), 123.1, 127.2, 128.5, 128.9, 132.5, 137.8, and 142.7 ($C_{aromatic}$), 166.8 (C(O)═N).

12b: 80.9 mg, 81%. Anal. Found: C, 62.49; H, 3.83; N, 5.63. Calcd for $C_{52}H_{38}N_4Cl_4O_2Pd$: C, 62.51; H, 3.83; N, 5.61. High-resolution ESI$^+$: *m*/*z* 1022.0775 ($[M + Na]^+$ requires 1022.0776). R_f = 0.41 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2933 m (C−H), 1630 s (C═N). δ_H (300 MHz, $CDCl_3$): 7.19, 7.43, 7.56, 7.72, 7.83 (5 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 98.3 (N−C−N), 121.0, 124.5, 127.5, 129.2, 132.3, 133.2, 135.1, and 141.2 ($C_{aromatic}$), 162.2 (C(O)═N).

13b: 44.2 mg, 91%. Anal. Found: C, 46.81; H, 5.53; N, 13.65. Calcd for $C_{24}H_{34}N_6Cl_2O_2Pd$: C, 46.80; H, 5.56; N, 13.65. High-resolution ESI$^+$: *m*/*z* 618.1328 ($[M + H]^+$ requires 618.1327). R_f = 0.40 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2935 m (C−H), 1666 s (C═N). δ_H (300 MHz, $CDCl_3$): 2.32 (3H, s, CH_3 from *p*-tol), 2.75 (3H, s, N(O)Me), 3.10 (6H, br s, NMe_2), 5.39 (1H, br s, CH), 7.19 (2H, two d, *m*-H from C_6H_4Me-*p*), 7.40 (2H, br d, *o*-H from C_6H_4Me-*p*). δ_C (75.5 MHz, $CDCl_3$): 21.7 (CH_3 from *p*-tol), 39.6 (NMe_2), 44.5 (N(O)Me), 93.4 (N−CH−N), 129.1, 130.2, 135.08, and 139.3 ($C_{aromatic}$), 158.6 (C(O)═N).

Reversibility Experiment and Characterization of ***14*** *and* ***15****.* A solution of **7b** (or **9b**) was stirred in $NCNMe_2$ for 48 h, and the progress of the reaction was monitored by TLC. Complexes **14** and **15** were isolated by column chromatography on SiO_2 (Merck, 70−230 mesh; eluent $CHCl_3/Me_2CO$ 40/1 v/v). The solvent was evaporated in vacuo at room temperature to give yellow oily residues, which were crystallized under *n*-hexane to form the yellow powders of **14** and **15**. The complexes were dried in air at 20−25 °C. Yields: 56−73%.

14: 48.2 mg, 56%. Anal. Found: C, 62.65; H, 5.01; N, 8.12. Calcd for $C_{45}H_{43}N_5Cl_2O_2Pd$: C, 62.62; H, 5.02; N, 8.11. High-resolution ESI$^+$: *m*/*z* 887.1821 ($[M + Na]^+$ requires 887.1821). R_f = 0.56 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2933 m (C−H), 1658 s (C═N). δ_H (300 MHz, CD_2Cl_2): 1.30 (3H, t, *J* = 7.6 Hz, CH_3 from Et), 2.20 (3H, s, CH_3 from C_6H_4Me-*p* of 5-Et-2,3-dihydro-1,2,4-oxadiazole ligand), 2.40 (3H, s, CH_3 from C_6H_4Me-*p* 5-Ph-2,3-dihydro-1,2,4-oxadiazole ligand), 2.81 (2H q, *J* = 7.6 Hz, CH_2 from Et), 3.08 (6H, br s, NMe_2), 6.46, 6.72, 7.18, 7.43, 7.63, 7.83 (28H, 6 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 10.0 (CH_3 from Et), 21.2 and 21.4 (CH_3 from C_6H_4Me-*p*), 22.6 (CH_2 from Et), 39.9 (NMe_2), 98.3 and 98.5 (N−C−N), 122.2, 126.7, 128.6, 128.8, 132.3, 132.8, 135.8, 136.2, 138.2, and 141.3 ($C_{aromatic}$), 161.2 (C(O)═N).

15: 67.4 mg, 73%. Anal. Found: C, 64.92; H, 4.90; N, 7.59. Calcd for $C_{50}H_{45}N_5Cl_2O_2Pd$: C, 64.91; H, 4.90; N, 7.57. High-resolution ESI$^+$: *m*/*z* 949.1979 ($[M + Na]^+$ requires 949.1977). R_f = 0.50 (eluent $CHCl_3/Me_2CO$, 40/1 v/v). IR ν_{max}/cm^{-1} (KBr): 2930 m (C−H), 1651 s (C═N). δ_H (300 MHz, CD_2Cl_2): 2.21 (6H, s, CH_3 from C_6H_4Me-*p* of 5-NMe_2-2,3-dihydro-1,2,4-oxadiazole ligand), 3.06 (3H, s, CH_3 from C_6H_4Me-*p* 5-Ph-2,3-dihydro-1,2,4-oxadiazole ligand), 3.06 (6H, br s, NMe_2), 6.40, 6.79, 7.20, 7.43, 7.55, 7.70, 7.82 (33H, 7 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 21.5 (CH_3 from C_6H_4Me-*p*), 2.40 (3H, t, CH_3 from *p*-tol), 39.9 (NMe_2), 98.5 and 98.3 (N−C−N), 121.1, 122.3, 125.0, 128.2, 128.9, 132.4, 135.8, 138.2, and 141.8 ($C_{aromatic}$), 162.0 and 162.3 (C(O)═N).

Liberation of 2,3-Dihydro-1,2,4-oxadiazole Ligands. dppe (2 equiv) was added to a solution of **7b**−**13b** in CH_2Cl_2, and the reaction mixture was stirred at room temperature for 4 h, whereupon the colorless $[Pd(dppe)_2](Cl)_2$[15] precipitated. The dichloromethane solutions of free 2,3-dihydro-1,2,4-oxadiazoles were filtrated off, and the solvent was evaporated in vacuo at room temperature to give oily residues of free heterocycles. Yields were almost quantitative.

Characterization of Metal-Free 2,3-Dihydro-1,2,4-oxadiazoles. **9c**. High-resolution ESI$^+$: *m*/*z* 392.1881 ($[M + H]^+$ requires 392.1883). R_f = 0.43 (eluent $CHCl_3/Me_2CO$, 50/1 v/v). δ_H (300 MHz, $CDCl_3$): 2.40 (3H, t, CH_3 from *p*-tol), 7.19, 7.43, 7.53, 7.70, 7.80 (19H, 5 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 10.1 (CH_3 from *p*-tol), 98.1 (N−C−N), 121.0, 124.6, 127.5, 129.0, 129.4, 132.1, 133.2, 135.1, and 141.0 ($C_{aromatic}$), 162.1 (C(O)═N).

10c. High-resolution ESI$^+$: *m*/*z* 386.1159 ($[M + Na]^+$ requires 386.1156). R_f = 0.44 (eluent $CHCl_3/Me_2CO$, 50/1, v/v). δ_H (300 MHz, $CDCl_3$): 1.30 (3H, t, *J* = 7.6 Hz, CH_3 from Et), 2.80 (2H, q, *J* = 7.6 Hz, CH_2 from Et), 6.49 (2H, d, *o*-protons from C_6H_4Cl-*p*), 6.87 (2H, d, *m*-protons from C_6H_4Cl-*p*), 7.32, and 7.50 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 9.9 (CH_3 from Et), 22.5 (CH_2 from Et), 98.1 (N−C−N), 123.3, 127.1, 128.3, 131.5, 132.5, 137.8, and 142.8 ($C_{aromatic}$), 160.1 (C(O)═N).

11c. High-resolution ESI$^+$: *m*/*z* 379.1440 ($[M + H]^+$ requires 379.1446). δ_H (300 MHz, $CDCl_3$): 3.01 (12H, br s, NMe_2), 6.40 (2H d, *o*-protons from C_6H_4Cl-*p*), 6.93 (2H, d, *m*-protons from C_6H_4Cl-*p*), 7.29, and 7.41 (10H, 2 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 39.8 (NMe_2), 98.2 (N−C−N), 123.1, 127.2, 128.7, 128.9, 132.6, 137.6, and 142.7 ($C_{aromatic}$), 166.7 (C(O)═N).

12c. High-resolution ESI$^+$: *m*/*z* 412.1335 ($[M + H]^+$ requires 412.1337). R_f = 0.41 (eluent $CHCl_3/Me_2CO$, 50/1, v/v). δ_H (300

dx.doi.org/10.1021/ic301866y | *Inorg. Chem.* XXXX, XXX, XXX−XXX

MHz, $CDCl_3$): 7.18, 7.40, 7.56, 7.71, 7.82 (5 m, $H_{aromatic}$). δ_C (75.5 MHz, $CDCl_3$): 97.2 (N−C−N), 121.0, 124.3, 127.5, 129.1, 132.2, 133.1, 135.1, and 141.2 ($C_{aromatic}$), 162.1 (C(O)=N).

■ ASSOCIATED CONTENT

Supporting Information

Tables, a figure, and a CIF file giving crystallographic data for **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Fax: +7 812 4286733. Tel: +7 812 4286890. E-mail: bokach@nb17701.spb.edu (N.A.B.); kukushkin@vk2100.spb.edu (V.Y.K.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Federal Targeted Program "Scientific and Scientific-Pedagogical Personnel of the Innovative Russia in 2009−2013" (Contract No. P1294 from 09/06/2010) and Russian Fund for Basic Research (Grant Nos. 11-03-00262 and 12-03-33071). We acknowledge St. Petersburg State University for a research grant (2011−2013; No. 12.37.133.2011) and a grant for applied research (2012−2013; No. 12.39.1050.2012). A.S.K. expresses his gratitude to the Government of St. Petersburg for a grant for graduate and undergraduate students (2011). Prof. A. P. Molchanov and Dr. T.Q. Tung are thanked for providing the ketonitrones for this study.

■ REFERENCES

(1) Kukushkin, V. Yu.; Pombeiro, A. J. L *Inorg. Chim. Acta* **2005**, *358* (1), 1−21.

(2) (a) Kukushkin, V. Yu.; Pombeiro, A. J. L. *Chem. Rev.* **2002**, *102* (5), 1771−1802. (b) Bokach, N. A.; Kuznetsov, M. L.; Kukushkin, V. Yu. *Coord. Chem. Rev.* **2011**, *255*, 2946−2967. (c) Kukushkin, V. Yu.; Bokach, N. A. *Russ. J. Gen. Chem.* **2007**, *77* (2), 194−205.

(3) (a) Michelin, R. A.; Mozzon, M.; Bertani, R. *Coord. Chem. Rev.* **1996**, *147*, 299−338. (b) Michelin, R. A.; Sgarbossa, P.; Sbovata, S. M.; Gandin, V.; Marzano, C.; Bertani, R. *ChemMedChem* **2011**, *6* (7), 1172−1183. (c) Ahmed, T. J.; Knapp, S. M. M.; Tyler, D. R. *Coord. Chem. Rev.* **2011**, *255* (7−8), 949−974. (d) Hvastijova, M.; Kohout, J.; Buchler, J. W.; Boca, R.; Kozisek, J.; Jager, L. *Coord. Chem. Rev.* **1998**, *175*, 17−42. (e) Eglin, J. L. *Comments Inorg. Chem.* **2002**, *23* (1), 23−43. (f) Tfouni, E.; Ferreira, K. Q.; Doro, F. G.; da Silva, R. S.; da Rocha, Z. N. *Coord. Chem. Rev.* **2005**, *249* (3−4), 405−418.

(4) (a) Kissane, M.; Maguire, A. R. *Chem. Soc. Rev.* **2010**, *2*, 845−883. (b) Stanley, L. M.; Sibi, M. P. *Chem. Rev.* **2008**, *108*, 2887−2902. (c) Broggini, G.; Molteni, G.; Terraneo, A.; Zecchi, G. *Heterocycles* **2003**, *59* (2), 823−858. (d) Gallos, J. K.; Koumbis, A. E. *Curr. Org. Chem.* **2003**, *7* (5), 397−425. (e) Karlsson, S.; Högberg, H.-E. *Org. Prep. Proced. Int.* **2001**, *33*, 103.

(5) (a) Bokach, N. A.; Kuznetsov, M. L.; Haukka, M.; Ovcharenko, V. I.; Tretyakov, E. V.; Kukushkin, V. Yu. *Organometallics* **2009**, *28* (5), 1406−1413. (b) Bokach, N. A.; Krokhin, A. A.; Nazarov, A. A.; Kukushkin, V. Yu.; Haukka, M.; Frausto Da Silva, J. J. R.; Pombeiro, A. J. L. *Eur. J. Inorg. Chem.* **2005**, *15*, 3042−3048. (c) Makarycheva-Mikhailova, A. V.; Golenetskaya, J. A.; Bokach, N. A.; Balova, I. A.; Haukka, M.; Kukushkin, V. Yu. *Inorg. Chem.* **2007**, *46* (20), 8323−8331. (d) Bokach, N. A.; Ioffe, S. L.; Dolgushin, F. M.; Antipin, M. Y.; Tartakovskii, V. A.; Kukushkin, V. Yu. *Inorg. Chem. Commun.* **2009**, *12* (2), 173−176. (e) Kritchenkov, A. S.; Bokach, N. A.; Haukka, M.; Kukushkin, V. Y. *Dalton Trans.* **2011**, *40* (16), 4175−4182. (f) Kritchenkov, A. S.; Bokach, N. A.; Kuznetsov, M. L.; Dolgushin, F. M.; Tung, T. Q.; Molchanov, A. P.; Kukushkin, V. Yu. *Organometallics* **2012**, *31* (2), 687−699.

(6) (a) Wagner, G.; Haukka, M. *Dalton Trans.* **2001**, *18*, 2690−2697. (b) Wagner, G.; Pombeiro, A. J. L.; Kukushkin, V. Y. *J. Am. Chem. Soc.* **2000**, *122* (13), 3106−3111. (c) Desai, B.; Danks, T. N.; Wagner, G. *Dalton Trans.* **2003**, 2544. (d) Desai, B.; Danks, T. N.; Wagner, G. *Dalton Trans.* **2004**, 166−171.

(7) (a) Lasri, J.; Charmier, M. A. J.; Haukka, M.; Pombeiro, A. J. L. *J. Org. Chem.* **2007**, *72* (3), 750−755. (b) Lasri, J.; Guedes da Silva, M. F. C.; Kopylovich, M. N.; Mukhopadhyay, S.; Charmier, M. A. J.; Pombeiro, A. J. L. *Dalton Trans.* **2009**, *12*, 2210−2216. (c) Lasri, J.; Kopylovich, M. N.; Guedes da Silva, M. F. C.; Charmier, M. A. J.; Pombeiro, A. J. L. *Chem. Eur. J.* **2008**, *14* (30), 9312−9322. (d) Charmier, M. A. J.; Kukushkin, V. Yu.; Pombeiro, A. J. L. *Dalton Trans.* **2003**, 2540−2543.

(8) (a) Beccalli, E. M.; Broggini, G.; La Rosa, C.; Passarella, D.; Pilati, T.; Terraneo, A.; Zecchi, G. *J. Org. Chem.* **2000**, *65*, 8924−8932. (b) Cordero, F. M.; Gensini, M.; Goti, A.; Brandi, A. *Org. Lett.* **2000**, *2*, 2475−2477. (c) Carmona, D.; Lamata, M. P.; Viguri, F.; Rodríguez, R.; Oro, L. A.; Balana, A. I.; Lahoz, F. J.; Tejero, T.; Merino, P.; Franco, S.; Montesa, I. *J. Am. Chem. Soc.* **2004**, *126*, 2716−2717. (d) Tamura, O.; Mita, N.; Okabe, T.; Yamaguchi, T.; Fukushima, C.; Yamashita, M.; Morita, Y.; Morita, N.; Ishibashi, H.; Sakamoto, M. *J. Org. Chem.* **2001**, *66*, 2602−2610. (e) Aggarwal, V. K.; Roseblade, S. J.; Barrell, J. K.; Alexander, R. *Org. Lett.* **2002**, *4*, 1227−1229. (f) Zhao, Q.; Han, F.; Romero, D. L. *J. Org. Chem.* **2002**, *67*, 3317−3322.

(9) (a) Bokach, N. A.; Kukushkin, V. Y. *Russ. Chem. Rev.* **2005**, *74* (2), 153−170. (b) Bokach, N. A.; Kukushkin, V. Y.; Haukka, M.; Pombeiro, A. J. L. *Eur. J. Inorg. Chem.* **2005**, *5*, 845−853. (c) Kuznetsov, M. L.; Kukushkin, V. Y.; Pombeiro, A. J. L. *Dalton Trans.* **2008**, *10*, 1312−1322. (d) Lasri, J.; Guedes da Silva, M. F. C.; Kopylovich, M. N.; Mukhopadhyay, S.; Charmier, M. A. J.; Pombeiro, A. J. L. *Dalton Trans.* **2009**, *12*, 2210−2216. (e) Wagner, G. *Inorg. Chim. Acta* **2004**, *357* (4), 1320−1324.

(10) Kuznetsov, M. L.; Kukushkin, V. Yu.; Pombeiro, A. J. L. *J. Org. Chem.* **2010**, *75*, 1474−1490.

(11) Pombeiro, A. J. L. *J. Organomet. Chem.* **2005**, *690* (24−25), 6021−6040.

(12) (a) Bertani, R.; Gotti, M.; Michelin, R. A.; Mozzon, M.; Bandoli, G.; Angelici, R. J. *Organometallics* **1996**, *15* (4), 1236−1241. (b) Leca, F.; Lescop, C.; Toupet, L.; Reau, R. *Organometallics* **2004**, *23* (26), 6191−6201.

(13) Liu, F. L.; Pullarkat, S. A.; Tan, K. W.; Li, Y. X.; Leung, P. H. *Organometallics* **2009**, *28*, 6254.

(14) Wagner, G. *Chem. Eur. J.* **2003**, *9* (7), 1503−1510.

(15) Kojima, T.; Saeki, K.; Ono, K.; Ohba, M.; Matsuda, Y. *Chem. Commun.* **1998**, *4*, 521−521.

(16) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, No. 12, S1−S19.

(17) (a) Sustmann, R. *Tetrahedron Lett.* **1971**, *12* (29), 2717−2720. (b) Sustmann, R. *Tetrahedron Lett.* **1971**, *12* (29), 2721−2724.

(18) (a) Kuznetsov, M. L. *Russ. Chem. Rev.* **2006**, *75* (11), 935−960. (b) Kuznetsov, M. L.; Kukushkin, V. Yu. *J. Org. Chem.* **2006**, *71* (2), 582−592. (c) Kuznetsov, M. L.; Kukushkin, V. Y.; Dement'ev, A. I.; Pombeiro, A. J. L. *J. Phys. Chem. A* **2003**, *107* (31), 6108−6120. (d) Kuznetsov, M. L.; Kukushkin, V. Y.; Pombeiro, A. J. L. *J. Org. Chem.* **2010**, *75* (5), 1474−1490. (e) Himo, F.; Demko, Z. P.; Noodleman, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **2003**, *125* (33), 9983−9987.

(19) Erxleben, A.; Mutikainen, I.; Lippert, B. *J. Chem. Soc., Dalton Trans.* **1994**, *24*, 3667−3675.

(20) (a) Svensson, P.; Lovqvist, K.; Kukushkin, V. Y.; Oskarsson, A. *Acta Chem. Scand.* **1995**, *49* (1), 72−75. (b) Bokach, N. A.; Pakhomova, T. B.; Kukushkin, V. Y.; Haukka, M.; Pombeiro, A. J. L. *Inorg. Chem.* **2003**, *42* (23), 7560−7568.

(21) Johnson, A. W. *J. Org. Chem.* **1963**, *28* (1), 252−254.

(22) Beckmann, E. *Liebigs Ann. Chem.* **1909**, *365*, 201−214.

(23) *APEX2-Software Suite for Crystallographic Programs*; Bruker AXS, Inc., Madison, WI, 2009.

(24) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Gualardi, A. *J. Appl. Crystallogr.* **1993**, *26* (3), 343−350.
(25) Farrugia, L. J. *J. Appl. Crystallogr.* **1999**, *32*, 837−838.
(26) Sheldrick, G. M. *SADABS-Bruker AXS Scaling and Absorption Correction*; Bruker AXS, Inc., Madison, WI, 2008.
(27) Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112−122.