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Pyridine-2(1*H*)-thione as a Bifunctional Nucleophile in Reaction with Pd^{II} and Pt^{II} Aryl Isocyanide Complexes

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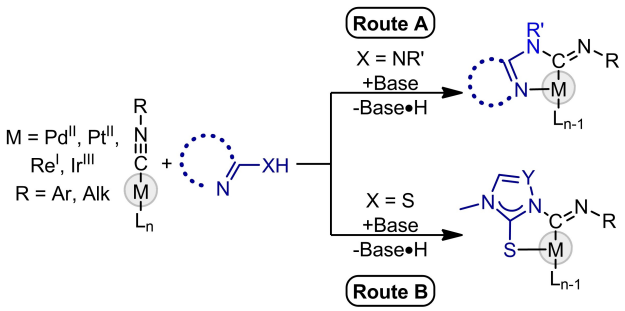
A method for obtaining *C,S*-cyclometalated deprotonated diaminocarbene complexes via the addition of a bifunctional *N,S*-nucleophile's endocyclic nitrogen atom to a coordinated isocyanide has been extended to the reactions with pyridine-2(1*H*)-thione. The coupling of Pd^{II}- and Pt^{II}-*bis*(arylisocyanide) complexes with pyridine-2(1*H*)-thione leads to the formation of mononuclear *C,S*- cyclometalated deprotonated diaminocarbene complexes in 90–96% yield. The reaction proceeds via the initial coordination of the thione sulfur atom to the metal center followed by the intramolecular nucleophilic addition of the heterocyclic nitrogen atom to the metal-ligated isocyanide carbon. Using excess of pyridine-2(1*H*)-thione in this reaction leads to the formation of a mono-*C,S*-cyclometalated complex with a pendant mercaptopyridine ligand which is involved in the reversible intramolecular nucleophilic addition of the pyridine nitrogen to the isocyano carbon. The obtained complexes were characterized by elemental analysis, mass spectrometry, IR and NMR spectroscopies, and single-crystal X-ray diffraction.

Introduction

The reactions of transition metals isocyanide complexes with *N*-nucleophiles are of constant interest to many chemists.[1–7] This interest is primarily associated with the preparation of transition metal acyclic diaminocarbene (ADC) complexes – the main products of this coupling in the case of using metal-coordinated isocyanides and mono-*N*-nucleophiles as substrates. Such complexes have promising catalytic properties,[2,3] and in some cases exhibit selective cytotoxic activity.[6,7] Moreover, if the used *N*-nucleophile contains an electrophilic center (or its synthetic equivalent), then the acyclic diaminocarbene species thus obtained can be converted into an NHC complex.[8,9]

Polyfunctional nucleophiles react with transition metals isocyanide complexes in a more complex manner. In this case, the type of the resulting product depends mainly on the structure of a nucleophile. This is especially true for derivatives of various azaheterocycles. In the case of 2-amino- (or 2-imino-) azoles and azines the reaction usually leads to the substitution of one of the anionic ligands with the formation of a *C,N*-cyclometalated complex (Route A, Scheme 1). Depending on the reaction conditions, the process can proceed further with the formation of more complex products [10–15], but all these nucleophiles afford to the reactions of a coordinated isocyanide with an exocyclic nucleophilic (amino-/imino-) group and the chelation of metal with a heterocyclic nitrogen atom.

Contrary, we found recently that the reaction of *bis*-(isocyanide) complexes of palladium(II) and platinum(II) with another type of nucleophiles – mercaptoazoles – proceeds in a completely different way.[16] This coupling leads to the formation of *C,S*-cyclometalated deprotonated diaminocarbene complexes (Route B, Scheme 1).



Scheme 1. The reaction of azaheterocyclic nucleophiles with isocyanide complexes.

The reason for this difference is the increased tendency of the sulfur atom (compare with the nitrogen atom) to coordinate with soft metal-centers as Pd^{II}/Pt^{II}. In this case, there is a significant change in the electron density distribution at the heterocyclic fragment. Of interest is the question of whether the reaction regioselectivity depends on the type of heterocycle and the degree of its aromaticity. Therefore, in this work, we studied pyridine-2(1*H*)-thione, a representative of six-membered azaheterocycles. The choice of this compound as an object of study is due to the fact that pyridine is noticeably more aromatic than pyrrole and imidazole.[17,18]

Results and Discussion

Reactions of ***1–3a,b*** *with one equivalent of pyridine-2(1H)-thione.* The coupling of Pd^{II}- and Pt^{II}- *bis*(arylisocyanide) complexes *cis*-$[M^{II}Cl_2(CNAr)_2]$ (Ar = Xyl (2,6-$Me_2C_6H_3$) **1a,b**, 4-Br-Xyl (2,6-Me_2-4-

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Mes-B), 19.31 (2C, $CH_3^{2,6}$, Mes-A), 20.06 (1C, CH_3^4, Mes-B), 21.26 (1C, CH_3^4, Mes-B), 116.44 (1C, C^5, pyridine), 126.72 (2C, $C^{2,6}$, Mes-A), 127.27 (1C, C^3, pyridine), 128.34 (2C, $C^{3,5}$, Mes-B), 128.46 (2C, $C^{3,5}$, Mes-A), 134.15 (2C, $C^{2,6}$, Mes-B), 134.42 (1C, C^4, Mes-A), 135.61 (1C, C^6, pyridine), 139.07 (1C, C^4, Mes-B), 141.78 (1C, C^4, pyridine), 146.96 (1C, C^1, Mes-A), 151.26 (1C, C^1, carbene), 171.40 (1C, C^2, pyridine). The signal of the isocyanide carbon atom and C^1 quaternary atom by Mes-B was not found even at high acquisition. ^{195}Pt NMR ($CDCl_3$, δ, ppm, *J*/Hz): −3947 (s, 1Pt).

7. Yield: 95 % (29 mg). Anal. calcd for $C_{25}H_{26}ClN_3PdS*0.67CH_2Cl_2$: C, 49.62; H, 3.87; N, 8.27, found: C, 49.40; H, 3.41; N, 8.31. HRESI$^+$-MS: calcd for $C_{28}H_{27}N_4PtS_2^+$ 678.1320, found m/z 678.1327 $[M+H]^+$. IR (KBr, selected bands, cm^{-1}): ν(C≡N) 2174 (s), ν(C=N) 1631 (m), ν(C=N) 1604 (m). ^{1}H NMR ($CDCl_3$, −20 °C, δ, ppm, *J*/Hz): 2.06 (s, 6H, CH_3, Xyl-A), 2.20 (s, 6H, CH_3, Xyl-B), 6.20 (t, 1H, H^4, Xyl-A, $^3J_{H-H}=6.9$), 6.67 (s, 1H, H^5, pyridine-B), 6.72 (d, 2H, $H^{3,5}$, Xyl-A, $^3J_{H-H}=6.9$), 6.88 (d, 2H, $H^{3,5}$, Xyl-B, $^3J_{H-H}=6.6$), 7.06 (m, 2H, H^5, pyridine-A and H^4, Xyl-B), 7.21 (s, 1H, H^3, pyridine-B), 7.51 (t, 1H, H^4, pyridine-B, $^3J_{H-H}=6.1$), 7.73 (m, 2H, $H^{3,4}$, pyridine-A), 8.16 (s, 1H, H^6, pyridine-B), 9.43 (d, 1H, H^6, pyridine-A, $^3J_{H-H}=6.1$). ^{13}C{^{1}H} NMR ($CDCl_3$, −20 °C, δ, ppm): 18.26 (2C, CH_3, Xyl-B), 19.27 (2C, CH_3, Xyl-A), 116.53 (1C, C^5, pyridine-A), 117.91 (1C, C^5, pyridine-B), 123.79 (1C, C^4, Xyl-A), 126.50 (2C, $C^{3,5}$, Xyl-B), 127.05 (2C, $C^{2,6}$, Xyl-A), 127.15 (1C, C^3, pyridine-A), 127.32 (2C, $C^{3,5}$, Xyl-A), 128.40 (1C, C^4, Xyl-B), 129.03 (1C, C^4, pyridine-B),133.66 (2C, $C^{2,6}$, Xyl-B), 135.59 (2C, C^6, pyridine-A and C^3, pyridine-B), 141.78 (1C, C^4, pyridine-A), 146.71 (1C, C^6, pyridine-B), 148.79 (1C, C^1, Xyl-A), 165.32 (1C, C^2, pyridine-B), 169.87 (1C, C^2, pyridine-A). The signals of the isocyanide carbon atom, C^1 carbene and the C^1 quaternary atom by Xyl-B were not found even at high acquisition. ^{195}Pt NMR ($CDCl_3$, δ, ppm, *J*/Hz): −4162 (s, 1Pt).

Single-crystal X-ray diffraction. The crystals of **4b**–**6b**, and **7** were obtained from dichloromethane solutions. For the single-crystal XRD experiment, suitable crystals of **4b**–**5b** were fixed on a micro mount, placed on an Agilent Technologies Xcalibur Eos diffractometer, and measured at 100 K by using monochromated Mo Kα radiation. Suitable crystals of **6b** and **7** were fixed on a micro mount, placed on an Agilent Technologies SuperNova diffractometer, and measured at 100 K, by using monochromated Cu Kα radiation. All structures were solved by direct methods using the SHELX program[34] incorporated in the OLEX2 program package.[35] **6b** contained a solvent from crystallization (CH_2Cl_2) that could not be unambiguously solved. Therefore, the contribution of the solvent to the calculated structure factors was taken into account by using the SQUEEZE routine. The H atoms were placed in calculated positions and were included in the refinement in the 'riding' model approximation, with U_{iso}(H) set to 1.5U_{eq}(C) and C–H 0.96 for CH_3 groups, with U_{iso}(H) set to 1.2U_{eq}(C) and C–H 0.93 Å for CH groups. The crystallographic data and some parameters of refinement are given in Table S1.

Computational details. The full geometry optimization of model structures **7** and **8** in a gas phase has been carried out at the DFT level of theory using the M06[36] functional with the empirical corrections for the dispersion in accordance with Grimme's D3 model[37] by Gaussian-16 program package.[38] For geometry optimization, the def2-TZVP basis set for all atoms was used.[39] The solvent effects were taken into account using the SMD continuum solvation model by Truhlar et al.[40] with $CHCl_3$ as solvent. No symmetry restrictions have been applied during the geometry optimization procedure. The Hessian matrices were calculated analytically for all optimized model structures to prove the location of correct minima on the potential energy surface (no imaginary frequencies were found). The NCI analysis was carried out using the Multiwfn 3.8 software[41] and visualized using the VMD software.[42] The Cartesian atomic coordinates for optimized equilibrium model structures are presented as XYZ-files in Supporting information.

Deposition Numbers 2113869 (for 4b), 2113870 (for 5b), 2113871 (for 6b), and 2181804 (for **7**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Cyclometalated complexes · Isocyanides · Platinum metals complexes · Pyridine-2(1*H*)-thione

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