www.elsevier.nl/locate/jorganchem

Journal of Organometallic Chemistry 622 (2001) 38–42

Journal of Organometallic Chemistry

Water-soluble cyclopalladated aryl oxime: a potent 'green' catalyst

Ekaterina Yu. Bezsoudnova, Alexander D. Ryabov *

Department of Chemistry, Moscow State University, 119899, Moscow, Russia

Received 13 September 2000; received in revised form 15 September 2000

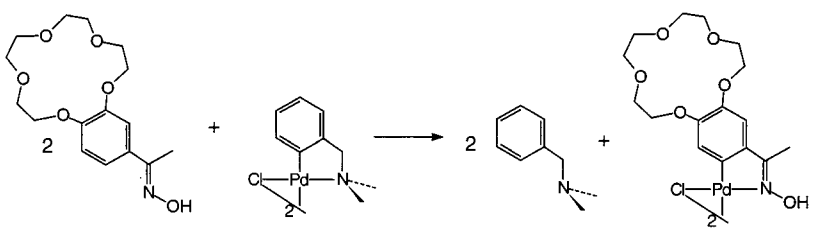
Abstract

Orthopalladated aryl oxime with a 15-crown-5 motif is prepared in a 72% yield by the exchange of cyclopalladated ligands from oxime of 4′-acetylbenzo-15-crown-5 and orthometalated *N*,*N*-dimethylbenzylamine, $[Pd(o\text{-}C_6H_4CH_2NMe_2)Cl]_2$. Its solubility in water is more than ten times higher than that of the related complex without the crown fragment and increases further in the presence of magnesium(II) salts. Potential applications of the newly synthesized palladacycle in catalysis is demonstrated by the example of biomimetic hydrolysis of 4-nitrophenyl 2,3-dihydroxybenzoate. It has been demonstrated that a 120-fold rate increase is achieved by realization of the intramolecular general base mechanism.

Keywords: Palladium; Cyclometalation; Ligand exchange; Crown ethers; Ester; Hydrolysis; Kinetics

1. Introduction

Chemistry of cyclopalladated complexes has recently got a new impulse. In addition to traditional applications of palladacycles as starting materials in fine organic synthesis [1–3], the compounds are nowadays frequently used as catalysts. Impressive progresses have been achieved in the Heck type reactions in which palladacycles proved to be extremely promising [4,5]. Very recently, the oxime palladacyles have been reported to be particularly efficient as catalysts of the Heck, Stille, Suzuki, and Ullmann reactions [6]. Our interests in catalytic applications of oxime pallada- and platinacycles are focused on mimicking of proteolytic [7–11] and redox enzymes [12]. However, low solubility of the metallacycles in aqueous media has hampered the progress in this field. Solubility in 'green' solvents such as water is essential not only for bioinorganic chemistry, but for industrial catalysis as well because of severe environmental regulations [13]. We are trying to increase the solubility of cyclometalated compounds in water since 1992 [14,15]. It was first decided to use pyridine-3-sulfonic acid as an extra ligand, the charge of which was thought to increase the solubility. However, there was no improvement, since the coordination of the py-3-SO_3^- ligand generated a zwitter-ionic species insufficiently soluble as well. Addition of charges cannot thus be necessarily successful, and uncharged hydrophilic groups should alternatively be used to make a metallacycle water-soluble. In this work, we demonstrate that the solubility in water is increased by attaching a 5-crown-15 motif to the orthopalladated aryl oxime and compound **1** becomes sufficiently soluble and catalyzes, for example, the hydrolysis of 4-nitrophenyl 2,3-dihydroxybenzoate, the



(1)

* Corresponding author. Fax: +7-095-9395417.
E-mail address: ryabov@enz.chem.msu.ru (A.D. Ryabov).

0022-328X/01/$ - see front matter
PII: S0022-328X(00)00825-1

analogs of which are used for the modeling of catalysis by serine proteases [16].

2. Experimental

2.1. General

Spectrophotometric and kinetic measurements were carried on a Hitachi 150-20 instrument with a thermostated by circulating water cell compartment. ^{1}H-NMR spectra were recorded on a CXP-200 Bruker instrument with a residual solvent signal as internal standard. Oxime of 4′-acetylbenzo-15-crown-5 was prepared as described elsewhere [17].

2.2. Synthesis of complex *1*

Complex **3** (0.138 g, 0.25 mmol) [18] was dissolved in 7 ml of $CHCl_3$ and 10 ml of HOAc and the oxime solution (0.162 g, 0.5 mmol) in 3 ml of $CHCl_3$ was added. The mixture was kept at 50°C for 48 h. Grey–yellow precipitate formed was filtered off, the filtrate concentrated to 5 ml using a rotary evaporator, complex **1** precipitated by slow addition of *n*-hexane, then filtered, washed with hexane, and air dried. ^{1}H-NMR (200 MHz, δ, $CDCl_3$, *J* in Hz): oxime of 4′-acetylbenzo-15-crown-5: 2.24(s, 3H, CH_3), 3.77(s, 8H, $^{8,9,11,12}CH_2$), 3.91(m, 4H, $^{6,14}CH_2$), 4.15(m, 4H, $^{5,15}CH_2$), 6.83(d, 1H, *J* 8, 5′H), 7.11(dd, 1H, *J* 8 and 2, 4′H), 7.23(d, 1H, *J* 2, 2′H), 8.75(bs, 1H, NOH). **1**: 1.88(s, 3H, CH_3), 3.79(s, 8H, $^{8,9,11,12}CH_2$), 3.95(m, 4H, $^{6,14}CH_2$), 4.20(m, 4H, $^{5,15}CH_2$), 6.23(s, 1H, 2′H), 7.05(s, 1H, 5′H), 8.45(s, 1H, NOH). Anal. Found: C, 40.6; N, 2.2; H, 4.9. Calc. for $[C_{19}H_{31}NO_6ClPd]_2$: C, 41.2; N, 3.0; H, 4.7%.

2.3. Kinetic and equilibrium measurements

The rate of hydrolysis of **4** was studied spectrophotometrically by monitoring the 4-nitrophenolate release at 405 nm [19]. The reactions were run at pH 8.0 (0.01 M phosphate buffer) and 25°C. Stock solutions of the Pd^{II} complexes and **4** were prepared in acetonitrile as solvent. The concentration of MeCN was maintained at a 6% level. Pseudo-first-order rate constants (k_{obs}) were calculated from the absorbance versus time (t) traces by plotting $\log(A_\infty/(A_\infty - A))$ against t. Each k_{obs} value is a mean value of at least three measurements.

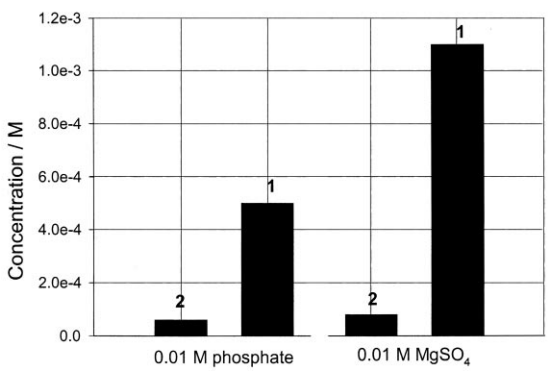


Fig. 1. Diagram showing solubilities of **1** and **2** in phosphate buffer pH 8.0 in the absence and in the presence of 0.01 M $MgSO_4$.

The equilibrium constants K_c for binding of catechol (L) with complexes **1** and **3** were obtained by measuring the absorbance changes at 308–320 nm at comparable concentrations of catechol and Pd^{II}. The profiles absorbance (A) versus catechol concentration were analyzed by fitting the experimental to the square equation

$$(A - \varepsilon_{Pd}[Pd^{II}])^2 - (A - \varepsilon_{Pd}[Pd^{II}])([Pd^{II}] + [L] + K_c)\Delta\varepsilon + [Pd^{II}][L]\Delta\varepsilon^2 = 0$$

where $\Delta\varepsilon = \varepsilon_{PdL} - \varepsilon_{Pd}$. All calculations were carried out using a SigmaPlot 4.00 package.

3. Results and discussion

3.1. Synthesis of complex *1*

Equation 1 shows the synthetic approach to complex **1**. The target compound **1** could not be obtained by reacting the oxime with K_2PdCl_4 in aqueous methanol. Poorly soluble grey–yellow material precipitated immediately at room temperature, presumably an N-coordinated species, since it dissolved only in excess of pyridine to give $[PdCl_2(py)_2]$ in accord with its ^{1}H-NMR spectrum. Other synthetic routines based on palladation of the C–H bond [20] were also not promising. Therefore, the exchange of cyclopalladated ligands was applied [21–23], which, as shown by us [24] and other workers [25], is very efficient for the synthesis of orthopalladated oximes. Dinuclear chloro-bridged dimer **1** was isolated in a 72% yield and characterized by the analytical data and the ^{1}H-NMR spectrum. The cyclopalladation of the C–H bond is proved by the observation of the two singlets in the aromatic region.

3.2. Solubility of complex *1* in water

The solubility of complex **1** in water was tested by adding stock solutions of **1** and its crown ether-free analogue $[Pd(o\text{-}C_6H_4C(Me)=NOH)Cl]_2$ (**2**) in MeCN to a buffered aqueous solution (pH 8.0, 0.01 M phosphate) with and without 0.01 M $MgSO_4$ (Fig. 1). The final concentration of MeCN in water did not exceed 6%. Maximal solubility of **2** at neutral pH in phosphate buffer was around 5×10^{-4} M. The radius of the inner cavity of 15-crown-5 equals 0.85 Å and should be compared with the ionic radii of Na^+, Mg^{2+} and Li^+ (1.02, 0.78 and 0.74 Å, respectively) [26]. The best

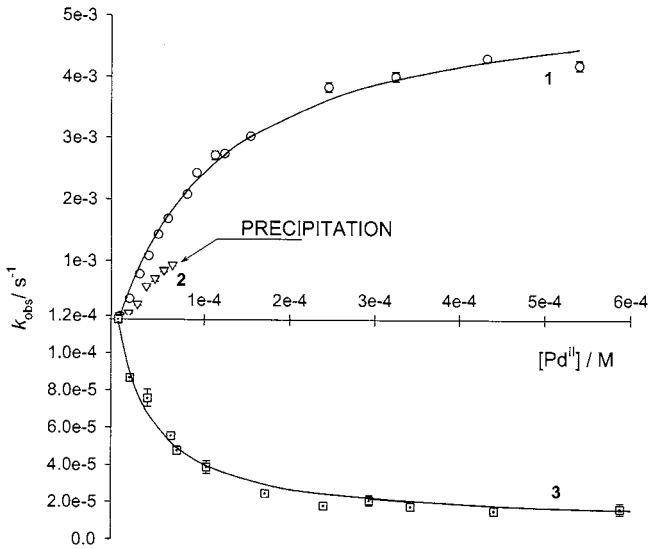
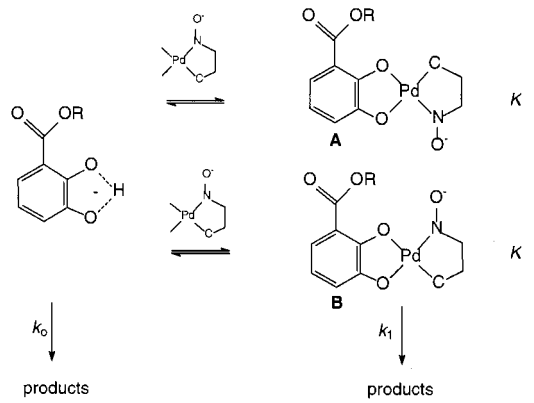


Fig. 2. Dependence of the observed pseudo-first-order rate constants for hydrolysis of **4** (2×10^{-5} M) against concentrations of **1**–**3** at pH 8.0 (phosphate buffer, 25°C).

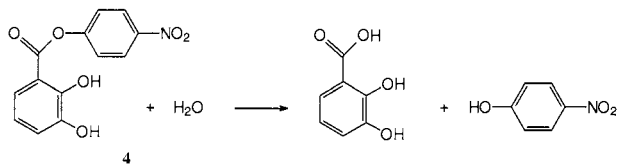


Scheme 1. Proposed mechanism of hydrolysis of 4-nitrophenyl 2,3-dihydroxybenzoate catalyzed be **1**.

correspondence between the cavity size and the ionic radius of Mg^{2+} and Li^{+} implies that **1** should be better soluble in the presence of these ions. In fact, the concentration of 1.1×10^{-3} M is easily achieved in 0.01 M $MgSO_4$. For comparison, the concentration of **2** is not higher 8×10^{-5} M under the same conditions.

3.3. Application of complex *1* in catalysis.

To illustrate advantages of using complex **1** as a catalyst, we have investigated palladacycles **1**–**3** as effectors of the biomimetic hydrolysis of 4-nitrophenyl 2,3-dihydroxybenzoate (**4**). Its vicinal hydroxy groups may serve as a trap for certain molecules which, on coordination, are capable of both increasing or decreasing the reaction rate and alter the intramolecular general base mechanism of hydrolysis of **4** [27,28]. Such a regulation of the reactivity by binding extra molecules makes **4** a functioning mimetic for the simulation of fine regulatory and/or allosteric effects encountered in the enzymatic systems [29,30]. On the other hand, metallacycles as *C,N*-chelates have a proper geometry for complexation with 1,2-diols. They exist in a monomeric form in MeCN and water and, hence, two *cis* coordinative sites are available for the complexation with the hydroxy groups of **4**. The binding of palladium(II) species with aromatic 1,2-diols is of precedent [31–33]. Therefore, the rate of hydrolysis of **4** (Eq. 2) has been investigated as a function of concentration of complexes **1**–**3**.



(2)

The dependencies of k_{obs} for reaction 2 against concentrations of palladacycles **1**–**3** are shown in Fig. 2. As seen, oxime complexes **1** and **2** accelerate the hydrolysis of **4**, whereas tertiary amine palladacycle **3** retards the rate. Remarkably, the k_{obs} values display the Michaelis type dependence and level off at higher concentrations of Pd^{II} indicative of the formation of reactive (**1** and **2**) and inactive (**3**) intermediates. The kinetic data is interpreted in terms of a general mechanism presented in Scheme 1 where **4** is shown as a semi-anion ($pK_a = 8.8$) [19]. Two types of oxime-diol palladium(II) complexes are depicted in Scheme 1. Obviously, only **B** is reactive, since the ester and oxime functionalities in complex **A** are too much separated to affect the ester cleavage.

On assumption that fast reversible formation of **A** and **B** is characterized by similar equilibrium constants K (Scheme 1), one arrives to the following rate expression for k_{obs}:

$$k_{obs} = \frac{k_o + nk_1K[Pd^{II}]}{1 + 2K[Pd^{II}]} \quad (3)$$

Here $n = 1$ for **1** and 2 for **3**. The data in Fig. 2 was fitted to Eq. (3) and the best-fit values of equilibrium and kinetic constants are summarized in Table 1.

As it was stated above, the hydrolysis of free **4** occurs via the intramolecular general base mechanism [19,28,34]. The complex formation between **4** and complex **3**, viz. palladacycle without nucleophile within the *C,N*-chelate, leads to diminishing the nucleophilic power of the semi-deprotonated 'intramolecular' base and the activation of water is no more feasible. As a result, there is the rate retardation by complex **3**. Complexes **1** and **2** accelerate the rate of hydrolysis of **4**. In contrast to **3**, these do have a strong extra nucleophile, viz. oximate ion, since the pK_a of the cyclopalladated

Table 1
Kinetic and equilibrium constants for hydrolysis of **4** in the presence of complexes **1** and **3** at pH 8 and 25°C.

Complex	k_o (M^{-1} s^{-1})	k_1 (M^{-1} s^{-1})	K (M^{-1})	K_c [a] (M^{-1})
1	$(1.2 \pm 0.1) \times 10^{-4}$	$(140 \pm 4) \times 10^{-4}$	$(0.38 \pm 0.02) \times 10^4$	$(0.25 \pm 0.12) \times 10^4$
3	$(1.2 \pm 0.1) \times 10^{-4}$	$(0.09 \pm 0.04) \times 10^{-4}$	$(1.1 \pm 0.1) \times 10^4$	$(3 \pm 1) \times 10^4$

[a] Obtained spectrophotometrically for catechol as unreactive analog of **4**.

aryl oximes is around 7–8 [24]. As a result, oximate rather than the hydroxo group functions as a general base (the measured solvent isotope effect $k(H_2O)/k(D_2O)$ equals 2.3 ± 0.2 at pD 9.0 and **1** 2.5×10^{-4} M), and since the nucleophilicity of the metalated aryl oximate is higher than that of the phenolic hydroxide, a significant catalysis by cyclopalladated aryl oximes is observed.

The mechanism proposed involving the *O,O′*-bonded intermediate is supported by the fact that hydrolysis of 4-nitrophenyl salicilate and benzoate is not catalyzed by **1** or **2** under the same conditions. Independent spectrophotometric measurements of the binding between catechol as an unreactive analog of **4**, on one hand, and **1** and **3**, on the other (low solubility precludes the measurements for **2** and the binding constant cannot also be extracted from the kinetic data in Fig. 2) are also in accord with the mechanism in Scheme 1. The effective values of the equilibrium constants K obtained for **1** and **3** from the kinetic data equal 0.38×10^4 and 1.1×10^4 M^{-1}, respectively. Spectrophotometric titration of **1** and **3** by catechol provided the K_c values of 0.25×10^4 and 3×10^4 M^{-1}, respectively. The values obtained in the kinetic and equilibrium experiments are quite comparable despite different molecules, i.e. **4** and catechol, were used. The coincidence is particularly striking for complex **1**. The mechanism in Scheme 1 is also in accord with the observations that platinum(II) analog of **2**, the complex [Pt(*o*-C_6H_4C(Me)=NOH)-Cl(py)], is catalytically inactive and does not show evidence for binding with catechol. It is also worth mentioning the magnitudes of both acceleration and retardation effects achieved in the presence of complexes **1** and **3**, respectively. The ratio of the rate constants k_1/k_o indicates that the coordinated palladated oxime **1** increases the rate 116-fold, whereas the inhibiting effect of **3** is a factor of 14. The entire range of the reactivity change is thus a factor of ca. 1600.

3.4. Conclusion

Sufficiently water soluble orthopalladated aryl oxime **1** obtained by the exchange of cyclopalladated ligands provided a possibility for equilibrium and kinetic studies of the catalyzed hydrolysis of **4** in a wide catalyst concentration range which cannot principally be accomplished for less the soluble aryl oxime complex **2**. This study has also demonstrated a potential of palladacycles in tuning the reactivity of biochemically relevant molecules and emphasized again that oximes are very promising ligands in creation of catalytic assemblies [35].

Acknowledgements

Financial support from the Russian Foundation for Basic Research (Grant No. 98-03-33023a) and INTAS (Project 97-0166) is gratefully acknowledged. We thank Drs I.K. Sakodinskaya and G.M. Kazankov for fruitful discussions and Dr V.A. Polyakov for the NMR measurements.

References

[1] A.D. Ryabov, Synthesis (1985) 233.
[2] M. Pfeffer, Recl. Trav. Chim. Pays-Bas 109 (1990) 567.
[3] J. Spencer, M. Pfeffer, in: L.S. Liebeskind (Ed.), Advances in Metal-Organic Chemistry, vol. 6, Jai Press, Stamford, 1998, p. 103.
[4] W.A. Herrmann, V.P.W. Böhm, C.-P. Reisinger, J. Organomet. Chem. 576 (1999) 23.
[5] I.P. Beletskaya, A.V. Cheprakov, Chem. Rev. 100 (2000) 3009.
[6] D.A. Alonso, C. Najera, M.C. Pacheco, Org. Lett. 2 (2000) 1823.
[7] E.V. Krooglyak, G.M. Kazankov, S.A. Kurzeev, V.A. Polyakov, A.N. Semenov, A.D. Ryabov, Inorg. Chem. 35 (1996) 4804.
[8] G.M. Kazankov, O.G. Dyachenko, A.V. Nemukhin, A.D. Ryabov, Mendeleev Commun. (1997) 159.
[9] A.D. Ryabov, G.M. Kazankov, S.A. Kurzeev, P.V. Samuleev, V.A. Polyakov, Inorg. Chim. Acta 280 (1998) 57.
[10] S.A. Kurzeev, G.M. Kazankov, A.D. Ryabov, Inorg. Chim. Acta 305 (2000) 1.
[11] G.M. Kazankov, V.S. Sergeeva, E.N. Efremenko, L. Alexandrova, S.D. Varfolomeev, A.D. Ryabov, Angew. Chem. Int. Ed. Engl. 39 (2000) 3117.
[12] L. Alexandrova, O.G. D'yachenko, G.M. Kazankov, V.A. Polyakov, P.V. Samuleev, E. Sansores, A.D. Ryabov, J. Am. Chem. Soc. 122 (2000) 5189.
[13] P.T. Anastas, J.C. Warner, Green Chemistry: Theory and Practice, Oxford University Press, Oxford, 1998.
[14] M. Schmülling, A.D. Ryabov, R. van Eldik, J. Chem. Soc. Chem. Commun. (1992) 1609.
[15] M. Schmülling, A.D. Ryabov, R. van Eldik, J. Chem. Soc. Dalton Trans. (1994) 1257.
[16] W.P. Jencks, Catalysis in Chemistry and Enzymology, Dover, New York, 1987.
[17] M. Tada, H. Hirano, A. Suzuki, Bull. Chem. Soc. Jpn. 53 (1980) 2304.
[18] A.D. Ryabov, V.A. Polyakov, A.K. Yatsimirsky, J. Chem. Soc. Perkin Trans. 2 (1983) 1503.

[19] A.K. Yatsimirsky, K.Y. Bezsoudnova, I.K. Sakodinskaya, Bioorg. Med. Chem. Lett. 3 (1993) 635.
[20] A.D. Ryabov, Chem. Rev. 90 (1990) 403.
[21] A.D. Ryabov, A.K. Yatsimirsky, Inorg. Chem. 23 (1984) 789.
[22] A.D. Ryabov, Inorg. Chem. 26 (1987) 1252.
[23] A.D. Ryabov, in: A.F. Williams, C. Floriani, A.E. Merbach (Eds.), Perspectives in Coordination Chemistry, VCH Weinheim, New York, 1992, p. 271.
[24] A.D. Ryabov, G.M. Kazankov, A.K. Yatsimirsky, L.G. Kuz'mina, O.Y. Burtseva, N.V. Dvortsova, V.A. Polyakov, Inorg. Chem. 31 (1992) 3083.
[25] K. Selvakumar, S. Vancheesan, B. Varghese, Polyhedron 16 (1997) 2257.
[26] S.A. Oehrle, J. Chromatogr. Sect. A 745 (1996) 87.
[27] M.L. Bender, F.J. Kezdy, B. Zerner, J. Am. Chem. Soc. 85 (1963) 3017.
[28] B. Capon, B.C. Ghosh, J. Chem. Soc. Sect. B (1966) 472.
[29] A. Fersht, Enzyme Structure and Mechanism, W.H. Freeman, San Francisco, 1977.
[30] J. Ricard, A. Cornish-Bowden, Eur. J. Biochem. 166 (1987) 255.
[31] O. Gandolfy, J. Blum, Inorg. Chim. Acta 80 (1983) 103.
[32] G.M. Kapteijn, A. Dervis, D.M. Grove, H. Kooijman, M.T. Lakin, A.L. Spek, G. van Koten, J. Am. Chem. Soc. 117 (1995) 10939.
[33] R. Roy, P. Chattopadhyay, C. Sinha, S. Chattopadhayay, Polyhedron 15 (1996) 3361.
[34] M.N. Khan, J. Mol. Catal. 40 (1987) 195.
[35] V.Y. Kukushkin, A.J.L. Pombeiro, Coord. Chem. Rev. 181 (1999) 147.