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Synthesis of osmium and ruthenium complexes bearing dimethyl (S,S)-2,2′-(pyridine-2,6-diyl)-bis-(4,5-dihydrooxazol-4-carboxylate) ligand and application to catalytic H/D exchange

Kenneth J.H. Young [a], Kapil S. Lokare [b,*], Chin Hin Leung [b], Mu-Jeng Cheng [c], Robert J. Nielsen [c,*], Nicos A. Petasis [a], William A. Goddard III [c], Roy A. Periana [b,**]

[a] Loker Hydrocarbon Institute, Department of Chemistry, University of Southern California, Los Angeles, CA 90089 USA
[b] The Scripps Research Institute, Scripps Florida, Jupiter, FL 33458, USA
[c] Materials and Process Simulation Center, California Institute of Technology, Pasadena, CA 91125, USA

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ABSTRACT

Using tridentate, neutral PyBox ligands, several new osmium and ruthenium complexes $[M(PyBox)Cl_2(C_2H_4)$, where M = Ru, Os] have been prepared, all thermally stable. Some of these PyBox compounds are active for C–H activation of benzene. The $Os(PyBox)Cl_2(C_2H_4)$ complex was characterized by X-ray diffraction. DFT calculations (B3LYP and M06 including Poisson–Boltzmann solvation) corroborate that the Os/PyBox complex in acetic acid ($\Delta G^{\ddagger} = 32.0$ kcal/mol) is more reactive for benzene C–H activation than Ru/PyBox in basic conditions ($\Delta G^{\ddagger} = 34.8$ kcal/mol at pH = 13). The stability of hydroxide- and chloride-bridged dinuclear resting states determines calculated barriers.

1. Introduction

The H/D exchange reaction has gained increased interest over the years as the need for labeled compounds has increased [1]. Target molecules can be selectively deuterated or tritiated for labeling studies in order to better understand and study reaction mechanism for both organic and organometallic reactions. It is also a useful tool for screening transition metal complexes as possible C–H activation catalysts. Our group [2] and others [3] have been interested in developing new catalytic systems for hydrocarbon hydroxylation. Previous C–H activation systems that our group has investigated involved electrophilic catalysts that operated in strongly acid media. Recently, we [4] and others [5] have been developing new systems that could potentially operate in weaker acidic media or non-acidic media.

Complexed to early transition metals [6,7] and lanthanides [8], 2,6-bis(2-oxazolin-2-yl)pyridine [9] {PyBox} has been widely used in Lewis Acid catalysis. Pybox complexes of transition metals have also been shown to act as catalysts for the polymerization of ethylene (Fe, Ru) [10], catalytic oxidations (Ru, Ir) [11], cyclopropanations (Ru) [12], hydrosilylations (Rh) [13] and transfer hydrogenations (Ru) [14].

In an interesting recent development, synthesis of water soluble Pybox ligands and their Fe(II) and Zn(II) complexes has been reported for use in asymmetric aqueous Mukaiyama-Aldol reactions [15]. In a related recent work, Odashima and co-workers [16] reported the synthesis of dimethyl (S,S)-2,2′-(pyridine-2,6-diyl)bis(4,5-dihydrooxazol-4-carboxylate) (**1a**) and dimethyl (S,S)-2,2′-(pyridine-2,6-diyl)bis(oxazole-4-carboxylate) (**1b**). We were interested in these ligands since upon hydrolysis they should become water soluble, and the carboxylate groups may assist in the C–H activation reaction as a pendant base [17]. In particular, we were interested if the ruthenium and osmium complexes of **1a**, and **1b** would undergo fast H/D exchange in acetic acid or in water. Complexes of ruthenium and osmium are expected to be less electrophilic for C–H activation and more tolerant of mildly acidic conditions [4c].

In this paper, we report the synthesis and characterization of water soluble ruthenium and osmium PyBox complexes (**2a-Cl$_2$** and **3a-Cl$_2$**), and their activity towards the H/D exchange reaction between benzene and either acetic acid-d_4 or D_2O.

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* Corresponding authors. Tel.: +1 561 228 2457; fax: +1 561 228 3064.
** Corresponding author.
E-mail addresses: klokare@scripps.edu (K.S. Lokare), smith@wag.caltech.edu (R.J. Nielsen), rperiana@scripps.edu (R.A. Periana).

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2. Experimental

2.1. General considerations

Unless otherwise noted all reactions were performed using standard Schlenk techniques under an atmosphere of argon or in an MBruan glove box under an atmosphere of purified nitrogen. Ultra high purity argon was used and passed through a column of Drierite. GC/MS analysis was performed on a Shimadzu GC-MS QP5000 (ver. 2) equipped with a cross-linked methyl silicone gum capillary column (DB5). ^{1}H (400 MHz), ^{13}C (100 MHz), and ^{19}F (376.5 MHz) NMR were collected on a Varian 400 Mercury plus spectrometer. Chemical shifts were referenced using residual protio solvent. Fluorine chemical shifts were referenced to $CFCl_3$. All coupling constants are reported in Hz. Mass spectrometry experiments were performed at UCR mass spectrometry laboratory or on an Applied Biosystems MALDI. Elemental analyses were performed by Columbia Analytical Services, Inc., Arizona. X-ray crystallography was collected on a Bruker SMART APEX CCD diffractometer. $[(p\text{-cymene})RuCl_2]_2$ (Strem), and $OsCl_3$ hydrate (Colonial metals) were used without purification. Dichloromethane was dried and degassed by sparging with argon then passing through an MBruan MB-SPS solvent purifier system. Anhydrous acetone was purchased from Aldrich and used as received. Ligands **1a** and **1b** were prepared following literature procedure [16].

2.2. Computational details

Geometries were optimized using the B3LYP [18] functional with a basis set of 6-31G** [19] for light atoms, and a double-ζ contraction of the Los Alamos valence functions and pseudopotentials [20] for metals. Analytic Hessians at these geometries provided the zero point energy and vibrational enthalpy and entropy. Solvation free energies G_{solv} were computed using the Poisson–Boltzmann polarizable continuum model with a dielectric constant of 80 and solvent radius of 1.4 Å for water, and a dielectric constant of 6.2 and solvent radius of 2.24 Å for acetic acid. The electronic energy E_{elec} was evaluated with the M06 [20,21] functional and the 6-311G**++ [22] basis and a triple-ζ contraction of the Los Alamos valence functions augmented with a diffuse *d* function and two *f*-functions [23].

Except the dimer dissociation reactions (**Ru-2** → **Ru-3** and **Os-1** → **Os-2**), Gibbs free energies of organometallic species at 1 M and 298 K were computed according to: $G = E_{\text{elec}} + G_{\text{solv}} + \text{ZPE} + 6\text{kT} + H_{\text{vib}} - \text{TS}_{\text{vib}}$, where 6kT is utilized to account for kinetic and potential energies of three translational and three rotational modes. In this expression, we assume that the translational and rotational entropies ($S_{\text{tran}} + S_{\text{rot}}$) for each organometallic species are the same, and therefore are cancelled, since for those reactions there is only one organometallic species in the reactant and product.

For the dimer dissociation reactions, we used $G = E_{\text{elec}} + G_{\text{solv}} + \text{ZPE} + 6\text{kT} + H_{\text{vib}} - T(S_{\text{vib}} + 0.5S_{\text{trans}} + 0.5S_{\text{rot}})$ to calculate the free energy of solutes, since there is one organometallic species in the reactants but two in the products (so that vibrational entropy does not cancel). Here, S_{trans} and S_{rot} are the translational and rotational entropies derived from the mass and moments of inertia using ideal gas statistical mechanics, and the empirical factor of 0.5 approximately relates vibrational entropy of solutes to their gas phase translational and rotational entropies.

The free energy of benzene at 1 atm was calculated according to ideal gas statistical mechanics, then corrected for the liquid phase using $\Delta G(1\,\text{atm} \to \text{liquid}) = -1.24$ kcal/mol (based on the vapor pressure of 0.12 atm at 298 K). Likewise, calculated free energies of hydroxide and water at 1 atm were corrected using the experimental values $\Delta G(H_2O,\ 1\,\text{atm} \to \text{liquid}) = -2.05$ kcal/mol [24] and $\Delta G(OH^-,\ 1\,\text{atm} \to 1\,\text{M}) = -103$ kcal/mol [25]. The pH-dependence of the hydroxide free energy was accounted for using $\text{pH} = 14 + \log[OH^-]$ and $\Delta G(OH^-, 1\,\text{M} \to [OH^-]) = -kT\ln(1\,\text{M}/[OH^-])$.

2.3. Preparation of Ru(II)(Pybox)(η^2–ethylene)Cl_2 (**2a**)

The ruthenium complex was synthesized following the general procedure established by Iwasa et al. [26] for a similar ligand. A 100 mL Schlenk bomb [27] was loaded with **1a** (400 mg, 1.2 mmol), $[(p\text{-cymene})RuCl_2]_2$ (367.5 mg, 0.6 mmol), and CH_2Cl_2 (40 mL). While stirring, ethylene was bubbled through the solution for 10 min. The Schlenk bomb was sealed and stirred at ambient temperature for 1 day. The solvent was removed and the resulting red solid was passed through silica gel with 15:1 CH_2Cl_2/MeOH, yielding 459.1 mg of **2a** (67.2% yield, avg. of 2 runs). ^{1}H NMR (400 MHz, $CDCl_3$): 8.01 (dd, 2H, ^3J = 8.9, 6.6 Hz, Py), 7.93 (dd, 1H, ^3J = 8.9, 6.6 Hz, Py), 5.21–5.13 (m, 6H, dihydrooxazole, C_2H_4), 5.08–4.98 (m, 4H, dihydrooxazole), 3.79 (s, 6H, CO_2Me). ^{13}C NMR (101 MHz, $CDCl_3$): 168.98, 166.82, 145.67, 133.57, 124.96, 75.29, 74.01, 67.10, 53.45. Anal. calcd. for $C_{17}H_{19}Cl_2N_3O_6Ru$: C, 38.28; H, 3.59; N, 7.88. Found C, 38.28; H, 3.66; N, 7.68. MALDI-MS (anthracene): calc. for $C_{15}H_{15}Cl_2N_3O_6Ru$ $(M-C_2H_4)^+$ 504.9; found 504.9.

2.4. Preparation of Os(II)(Pybox)(η^2–ethylene)Cl_2 (**3a**)

The osmium complex was synthesized following the general procedure established by Maitlis [28] for a similar ligand. A 100 mL Schlenk bomb was loaded with **1a** (331 mg, 0.99 mmol), $[(p\text{-cymene})OsCl_2]_2$ (393 mg, 0.50 mmol), and CH_2Cl_2 (10 mL). While stirring, ethylene was bubbled through the solution for 10 min. The Schlenk bomb was sealed and stirred at ambient temperature for 1 day. The solvent was removed and the resulting purple solid was passed through silica gel with 30:1 CH_2Cl_2/MeOH, yielding 312 mg of *trans*-**Cl-3a** (50.8% yield) and 107.2 mg of *cis*-**Cl-3a** (17.5% yield). ^{1}H NMR for *trans*-**Cl-3a** (400 MHz, $CDCl_3$): 7.49 (d, 2H, *J* = 7.9 Hz, Py), 7.15 (t, 1H, *J* = 7.9 Hz, Py), 5.34 (dd, 2H *J* = 9.1 Hz, dihydrooxazole), 5.26 (dd, 2H, *J* = 9.1, 5.5 Hz, dihydrooxazole), 5.26 (dd, 2H, *J* = 9.0, 5.5 Hz, dihydrooxazole), 5.06 (dd, 2H, *J* = 10.0, 5.5 Hz, dihydrooxazole), 4.78 (d, 2H, *J* = 11.3 Hz, C_2H_4), 4.57 (d, 2H, *J* = 11.3 Hz, C_2H_4), 3.79 (s, 6H, CO_2Me). ^{13}C NMR for *trans*-**Cl-3a** (101 MHz, $CDCl_3$): 171.59, 168.53, 138.27, 128.52, 123.76, 75.33, 68.13, 56.93, 53.45. Anal. calcd. for $C_{17}H_{19}Cl_2N_3O_6Os$ (*trans*-**3a**): C, 32.80; H, 3.08; N, 6.75. Found C, 32.91; H, 3.36; N, 6.26. HRESI-MS of *trans*-**Cl-3a**: calc. for $C_{17}H_{19}N_3O_6Cl_2Os$ 623.0266, found 623.0260 (M)+; calc. for $C_{17}H_{19}Cl_2N_3NaO_6Os$ 646.0163, found 646.0149 $(M+Na)^+$. ^{1}H NMR for *cis*-**Cl-3a** (400 MHz, $CDCl_3$): 7.55 (dd, 1H, *J* = 7.9, 1.1 Hz, Py), 7.52 (dd, 1H, *J* = 7.9, 1.4 Hz, Py), 7.06 (t, 1H, *J* = 7.9 Hz, Py), 5.50 (t, 1H, *J* = 8.3 Hz, dihydrooxazole), 5.27 (dd, 1H, *J* = 10.4, 8.9 Hz, dihydrooxazole), 5.12 (t, 2H, *J* = 8.6 Hz, dihydrooxazole), 4.95 (dd, 1H, *J* = 10.3, 8.6 Hz, dihydrooxazole), 3.90 (s, 3H, CO_2Me), 3.87 (s, 3H, CO_2Me), 3.03 (d, 2H, *J* = 8.5 Hz, C_2H_4), 2.78 (d, 2H, *J* = 8.5 Hz, C_2H_4). ^{13}C NMR for *cis*-**Cl-3a** (101 MHz, $CDCl_3$): 176.57, 175.82, 169.80, 167.55, 150.76, 150.55, 129.26, 129.02, 123.86, 75.78, 75.17, 66.86, 66.00, 58.30, 54.06, 53.66. Anal. calcd. for $C_{17}H_{19}Cl_2N_3O_6Os$ (*cis*-**3a**): C, 32.80; H, 3.08; N, 6.75. Found C, 31.25; H, 2.99; N, 6.44. HRESI-MS for *cis*-**Cl-3a**: 641.0585 $(M+NH_4)$+, 646.0147 $(M+Na)^+$.

2.5. Thermolysis of trans-**3a-Cl₂** in CD_3CN

In the glove box, a J-Young tube was loaded with *trans*-**3a-Cl$_2$** (~3 mg) in CD_3CN. ^{1}H NMR before heating shows *trans*-**3a-Cl$_2$**. Heated at 160 °C for 1 h. ^{1}H NMR (400 MHz, CD_3CN): 6.99 (d, 2H, *J* = 7.9 Hz, Py), 6.18 (t, 1H, *J* = 7.9 Hz, Py), 5.48 (dd, 2H, *J* = 9.2, 6.7 Hz, dihydrooxazole), 5.31 (t, 1H, *J* = 9.2, dihydrooxazole), 4.71 (dd, 1H, *J* = 9.7, 6.7 Hz, dihydrooxazole), 3.77 (s, 6H, *J* = 1.7 Hz, CO_2Me).