



# 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

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## ABSTRACT

Using tridentate, neutral PyBox ligands, several new osmium and ruthenium complexes [M(PyBox)Cl<sub>2</sub>(C<sub>2</sub>H<sub>4</sub>), 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<sub>2</sub>(C<sub>2</sub>H<sub>4</sub>) 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.

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## 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<sub>2</sub>** and **3a-Cl<sub>2</sub>**), and their activity towards the H/D exchange reaction between benzene and either acetic acid-*d*<sub>4</sub> or D<sub>2</sub>O.

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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).  $^1\text{H}$  (400 MHz),  $^{13}\text{C}$  (100 MHz), and  $^{19}\text{F}$  (376.5 MHz) NMR were collected on a Varian 400 Mercury plus spectrometer. Chemical shifts were referenced using residual proton solvent. Fluorine chemical shifts were referenced to  $\text{CFCl}_3$ . 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*-cymene] $\text{RuCl}_2$  (Strem), and  $\text{OsCl}_3$  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- $\zeta$  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  $G_{\text{solv}}$  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  $E_{\text{elec}}$  was evaluated with the M06 [20,21] functional and the 6-311G\*\*++ [22] basis and a triple- $\zeta$  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**  $\rightarrow$  **Ru-3** and **Os-1**  $\rightarrow$  **Os-2**), Gibbs free energies of organometallic species at 1 M and 298 K were computed according to:  $G = E_{\text{elec}} + G_{\text{solv}} + \text{ZPE} + 6kT + H_{\text{vib}} - TS_{\text{vib}}$ , 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  $G = E_{\text{elec}} + G_{\text{solv}} + \text{ZPE} + 6kT + H_{\text{vib}} - T(S_{\text{vib}} + 0.5S_{\text{trans}} + 0.5S_{\text{rot}})$  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,  $S_{\text{trans}}$  and  $S_{\text{rot}}$  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  $\Delta G(1 \text{ atm} \rightarrow \text{liquid}) = -1.24 \text{ kcal/mol}$  (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

$\Delta G(\text{H}_2\text{O}, 1 \text{ atm} \rightarrow \text{liquid}) = -2.05 \text{ kcal/mol}$  [24] and  $\Delta G(\text{OH}^-, 1 \text{ atm} \rightarrow 1 \text{ M}) = -103 \text{ kcal/mol}$  [25]. The pH-dependence of the hydroxide free energy was accounted for using  $\text{pH} = 14 + \log[\text{OH}^-]$  and  $\Delta G(\text{OH}^-, 1 \text{ M} \rightarrow [\text{OH}^-]) = -kT \ln(1 \text{ M}/[\text{OH}^-])$ .

### 2.3. Preparation of $\text{Ru(II)(Pybox)(}\eta^2\text{-ethylene)Cl}_2$ (**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*-cymene] $\text{RuCl}_2$  (367.5 mg, 0.6 mmol), and  $\text{CH}_2\text{Cl}_2$  (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  $\text{CH}_2\text{Cl}_2/\text{MeOH}$ , yielding 459.1 mg of **2a** (67.2% yield, avg. of 2 runs).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 8.01 (dd, 2H,  $^3J = 8.9, 6.6 \text{ Hz}$ , Py), 7.93 (dd, 1H,  $^3J = 8.9, 6.6 \text{ Hz}$ , Py), 5.21–5.13 (m, 6H, dihydrooxazole,  $\text{C}_2\text{H}_4$ ), 5.08–4.98 (m, 4H, dihydrooxazole), 3.79 (s, 6H,  $\text{CO}_2\text{Me}$ ).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ): 168.98, 166.82, 145.67, 133.57, 124.96, 75.29, 74.01, 67.10, 53.45. Anal. calcd. for  $\text{C}_{17}\text{H}_{19}\text{Cl}_2\text{N}_3\text{O}_6\text{Ru}$ : C, 38.28; H, 3.59; N, 7.88. Found C, 38.28; H, 3.66; N, 7.68. MALDI-MS (anthracene): calc. for  $\text{C}_{15}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_6\text{Ru} (\text{M}-\text{C}_2\text{H}_4)^+$  504.9; found 504.9.

### 2.4. Preparation of $\text{Os(II)(Pybox)(}\eta^2\text{-ethylene)Cl}_2$ (**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*-cymene] $\text{OsCl}_2$  (393 mg, 0.50 mmol), and  $\text{CH}_2\text{Cl}_2$  (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  $\text{CH}_2\text{Cl}_2/\text{MeOH}$ , yielding 312 mg of *trans*-**Cl-3a** (50.8% yield) and 107.2 mg of *cis*-**Cl-3a** (17.5% yield).  $^1\text{H}$  NMR for *trans*-**Cl-3a** (400 MHz,  $\text{CDCl}_3$ ): 7.49 (d, 2H,  $J = 7.9 \text{ Hz}$ , Py), 7.15 (t, 1H,  $J = 7.9 \text{ Hz}$ , Py), 5.34 (dd, 2H,  $J = 9.1 \text{ Hz}$ , dihydrooxazole), 5.26 (dd, 2H,  $J = 9.1, 5.5 \text{ Hz}$ , dihydrooxazole), 5.26 (dd, 2H,  $J = 9.0, 5.5 \text{ Hz}$ , dihydrooxazole), 5.06 (dd, 2H,  $J = 10.0, 5.5 \text{ Hz}$ , dihydrooxazole), 4.78 (d, 2H,  $J = 11.3 \text{ Hz}$ ,  $\text{C}_2\text{H}_4$ ), 4.57 (d, 2H,  $J = 11.3 \text{ Hz}$ ,  $\text{C}_2\text{H}_4$ ), 3.79 (s, 6H,  $\text{CO}_2\text{Me}$ ).  $^{13}\text{C}$  NMR for *trans*-**Cl-3a** (101 MHz,  $\text{CDCl}_3$ ): 171.59, 168.53, 138.27, 128.52, 123.76, 75.33, 68.13, 56.93, 53.45. Anal. calcd. for  $\text{C}_{17}\text{H}_{19}\text{Cl}_2\text{N}_3\text{O}_6\text{Os}$  (*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  $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_6\text{Cl}_2\text{Os}$  623.0266, found 623.0260 (M)<sup>+</sup>; calc. for  $\text{C}_{17}\text{H}_{19}\text{Cl}_2\text{N}_3\text{NaO}_6\text{Os}$  646.0163, found 646.0149 (M+Na)<sup>+</sup>.  $^1\text{H}$  NMR for *cis*-**Cl-3a** (400 MHz,  $\text{CDCl}_3$ ): 7.55 (dd, 1H,  $J = 7.9, 1.1 \text{ Hz}$ , Py), 7.52 (dd, 1H,  $J = 7.9, 1.4 \text{ Hz}$ , Py), 7.06 (t, 1H,  $J = 7.9 \text{ Hz}$ , Py), 5.50 (t, 1H,  $J = 8.3 \text{ Hz}$ , dihydrooxazole), 5.27 (dd, 1H,  $J = 10.4, 8.9 \text{ Hz}$ , dihydrooxazole), 5.12 (t, 2H,  $J = 8.6 \text{ Hz}$ , dihydrooxazole), 4.95 (dd, 1H,  $J = 10.3, 8.6 \text{ Hz}$ , dihydrooxazole), 3.90 (s, 3H,  $\text{CO}_2\text{Me}$ ), 3.87 (s, 3H,  $\text{CO}_2\text{Me}$ ), 3.03 (d, 2H,  $J = 8.5 \text{ Hz}$ ,  $\text{C}_2\text{H}_4$ ), 2.78 (d, 2H,  $J = 8.5 \text{ Hz}$ ,  $\text{C}_2\text{H}_4$ ).  $^{13}\text{C}$  NMR for *cis*-**Cl-3a** (101 MHz,  $\text{CDCl}_3$ ): 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  $\text{C}_{17}\text{H}_{19}\text{Cl}_2\text{N}_3\text{O}_6\text{Os}$  (*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<sub>4</sub>)<sup>+</sup>, 646.0147 (M+Na)<sup>+</sup>.

### 2.5. Thermolysis of *trans*-**3a-Cl**<sub>2</sub> in $\text{CD}_3\text{CN}$

In the glove box, a J-Young tube was loaded with *trans*-**3a-Cl**<sub>2</sub> (~3 mg) in  $\text{CD}_3\text{CN}$ .  $^1\text{H}$  NMR before heating shows *trans*-**3a-Cl**<sub>2</sub>. Heated at 160 °C for 1 h.  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{CN}$ ): 6.99 (d, 2H,  $J = 7.9 \text{ Hz}$ , Py), 6.18 (t, 1H,  $J = 7.9 \text{ Hz}$ , Py), 5.48 (dd, 2H,  $J = 9.2, 6.7 \text{ Hz}$ , dihydrooxazole), 5.31 (t, 1H,  $J = 9.2$ , dihydrooxazole), 4.71 (dd, 1H,  $J = 9.7, 6.7 \text{ Hz}$ , dihydrooxazole), 3.77 (s, 6H,  $J = 1.7 \text{ Hz}$ ,  $\text{CO}_2\text{Me}$ ).

## 2.6. Synthesis of dimethyl (*S,S*)-2,2'-(pyridine-2,6-diyl)bis(oxazole-4-carboxylate)( $\eta^2$ -ethylene) osmium (II) dichloride (**3b**)

A Schlenk bomb containing **1b** (500 mg, 1.52 mmol) and  $\text{OsCl}_3(\text{H}_2\text{O})_3$  (532.5 mg, 1.52 mmol) in EtOH (80 mL) was heated at 90 °C for 9 h. The solution was filtered over celite and washed with MeOH. The filtrate was allowed to run through a silica preparative TLC plate with DCM/MeOH (30:1). Yielding 40.4 mg of **3b**.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 9.45 (s, 2H), 8.81 (s, 2H, oxazole), 7.57 (d, 2H,  $J=7.9$  Hz, Py), 6.39 (t, 1H,  $J=7.9$  Hz, Py), 4.08 (s, 6H,  $\text{CO}_2\text{Me}$ ). ESI-MS of **3b**: 608.97 ( $\text{M}^+$ ), 622.99 ( $\text{M}-\text{H}_2\text{O}+\text{CH}_3\text{OH}^+$ ). Anal. calcd. for  $\text{C}_{15}\text{H}_{13}\text{Cl}_2\text{N}_3\text{O}_7\text{Os}$ : C, 29.61; H, 2.15; Cl, 11.65; N, 6.91. Found C, 29.49; H, 1.88; Cl, 11.90; N, 6.43.

## 2.7. Halide abstraction from **2a-Cl<sub>2</sub>**

A Schlenk bomb was loaded with **2a-Cl<sub>2</sub>** (472.0 mg, 0.885 mmol), and AgOTf (477.5 mg, 1.859 mmol) in 80 mL of MeOH was heated at 70 °C for 7 h in the dark. The resulting AgCl was filtered over celite, and washed with MeOH. The volatiles were removed under *vacuo*. The resulting red-brown solid was redissolved in minimal amount of acetone then precipitated from ether (300 mL). The solid was then dried under vacuum overnight to afford 594.8 mg of the desired product. The product has been assigned as the (Pybox)Ru(II)(OTf)<sub>2</sub>L complex (L = H<sub>2</sub>O or acetone) based on MALDI-MS. MALDI-MS (anthracene). 750.0 ( $\text{M}^+$ ), 732.9 ( $\text{M}-\text{H}_2\text{O}^+$ ), 583.9 ( $\text{M}-\text{OTf}-\text{H}_2\text{O}^+$ ). Anal. calcd. for  $\text{C}_{17}\text{H}_{17}\text{F}_6\text{N}_3\text{O}_{13}\text{RuS}_2(\text{OC}(\text{CH}_3)_2(\text{H}_2\text{O}))$ : C, 29.06; H, 3.05; F, 13.79; N, 5.08. Found C, 29.43; H, 2.87; F, 13.15; N, 5.42.

## 2.8. Halide abstraction form *trans*-**3a-Cl<sub>2</sub>**

A solution of *trans*-**3a-Cl<sub>2</sub>** (565.4 mg, 0.908 mmol) in acetone (2 mL) was added TlPF<sub>6</sub> (634.6 mg, 1.817 mmol) in 20 mL of anhydrous acetone and was stirred for 4 days. The suspension was filtered over celite and washed with acetone. The volatiles were removed under *vacuo*. The resulting solid was washed with  $\text{CH}_2\text{Cl}_2$ , extracted with acetone, filtered over celite, then reprecipitated with benzene. The volatiles were then removed under *vacuo*. The product has been assigned as the [(Pybox)Os(II)Cl(acetone)]PF<sub>6</sub> complex.  $^1\text{H NMR}$  (400 MHz, acetone): 7.66 (d, 2H  $J=7.9$  Hz, Py), 7.35 (t, 1H,  $J=7.9$  Hz, Py), 5.48 (m, 4H, dihydrooxazole), 5.08 (dd, 2H,  $J=7.8, 6.6$  Hz, dihydrooxazole), 4.77 (d, 2H,  $J=11.1$  Hz,  $\text{C}_2\text{H}_4$ ), 4.39 (d, 2H,  $J=11.1$  Hz,  $\text{C}_2\text{H}_4$ ), 3.66 (s, 6H,  $\text{CO}_2\text{Me}$ ). ESI-MS calc. for  $\text{C}_{20}\text{H}_{25}\text{ClN}_3\text{O}_7\text{Os}$  ( $\text{M}-\text{PF}_6^+$ ): 646.10; found 646.01. ESI-MS Calculated for  $\text{C}_{18}\text{H}_{23}\text{ClN}_3\text{O}_7\text{Os}$  ( $\text{M}-\text{PF}_6-\text{L}+\text{MeOH}^+$ ): 620.08; found 620.07.

## 2.9. H/D exchange studies

Catalytic H/D exchange reactions were quantified by monitoring the increase of deuterium into  $\text{C}_6\text{H}_6$  by GC-MS analyses. This was achieved by deconvolution of the mass fragmentation pattern obtained from the MS analysis, using a program developed with Microsoft EXCEL [29]. An important assumption used in the program is that there are no isotope effects on the fragmentation pattern of the benzenes due to replacement of H with D. Fortunately, because of the relative stability of the parent ion towards fragmentation, it can be used reliably to quantify the exchange reactions. The mass range from 78 to 84 (for benzene) was examined for each reaction and compared to a control reaction where no metal catalyst was added. The program was calibrated with known mixtures of benzene isotopologues. The results obtained from this method are reliable within 5%.

## 2.10. H/D exchange experiments

In a typical experiment, a homogeneous solution of complex **2a-OTf<sub>2</sub>**, or **3a-Cl** (10–15 mg) in a benzene/DX solvent mixture (X = OD (1:1 mL), OAc- $d_3$  (0.2:1 mL)) with or without zinc mesh (~60 mg) was heated at 170 °C in a Schlenk bomb. After the reaction was complete the Schlenk bomb was cooled to room temperature. The liquid phase was then analyzed by GC-MS to determine extent of H/D exchange. TON was calculated as moles of product/moles of catalyst (where moles of product = moles of D1  $\times$  1 + moles of D2  $\times$  2 + moles of D3  $\times$  3 + moles of D4  $\times$  4 + moles of D5  $\times$  5 + moles of D6  $\times$  6). Control runs between benzene/acetic acid- $d_3$ , and benzene/D<sub>2</sub>O both with or without zinc mesh showed no background H/D exchange.

## 2.11. X-ray crystallography

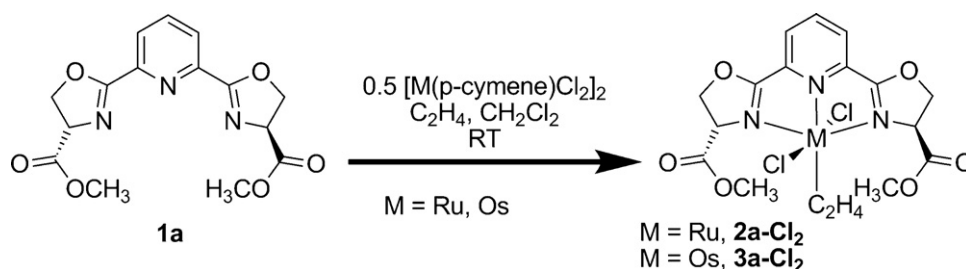
Diffraction data on a purple needle of the **3a-Cl<sub>2</sub>** were collected at 128 K on a SMART APEX CCD diffractometer with graphite fine-focused monochromatic Mo- $\text{K}\alpha$  radiation ( $\lambda=0.71073$  Å). The cell parameters for **3a-Cl<sub>2</sub>** were obtained from the least-squares refinement of the spots (from 60 collected frames) using the SMART program on a single crystal sample measuring 0.17 mm  $\times$  0.10 mm  $\times$  0.08 mm. A hemisphere of data was collected up to a resolution of 0.77 Å and the intensity data were processed using the "Saint Plus" program. All calculations for the structure determination were carried out using the SHELXTL package (version 6.14) [30]. Initial positions of the osmium atoms were located by a Patterson function using the program XS. The remaining atoms were located in the difference-Fourier maps, refined by least squares using SHELX with 12,619 independent reflections within the range of  $\theta$  1.3–27.5° (completeness 99.5%). Absorption corrections were applied by SADABS [31,2], with an  $R_{(\text{int})}=7.5\%$ . Calculated hydrogen positions were input and refined in a riding manner along with the corresponding carbons.

Final structure refinement for **3a-Cl<sub>2</sub>** resulted in a  $R_1=3.7\%$  and  $wR_2=7.4\%$ . The data to parameter ratio is 18:1. The crystal system found is tetragonal, space group  $\text{P4}_32_12$ , with  $Z$  equal to 20 and unit cell dimensions:  $a=20.79$  Å,  $b=20.79$  Å,  $c=25.64$  Å. There are two and a half molecules in the asymmetric unit, in which one osmium atom is situated on a twofold rotational axis, while the other two osmium molecules are in general positions. This un-common number of molecules ( $Z=20$ ) in a tetragonal space group raised our attention as to the validity of the assignment. We found the primitive tetragonal assignment to be correct after careful examination of the  $hkl$  intensities and verifying the systematic extinctions of  $h00=0k0=2n$  and  $00l=4n$  consistent with either space group  $\text{P4}_32_12$  (#96) or  $\text{P4}_12_12$  (#92) [32]. Refinement was then carried out in the alternative mirror image space group  $\text{P4}_12_12$  (#92), but with inferior results. Hence, we conclude that original assignment of  $Z=20$  in space group  $\text{P4}_32_12$  is in fact correct.

There are three water molecules located in the crystal lattice which can be rationalized by the fact that our samples were grown while exposed to the atmosphere. In addition, two solvent molecules which appeared to be methanol were also found in the unit cell but methanol refined poorly using anisotropic parameters therefore the molecule was refined isotropically.

## 3. Results and discussion

The water soluble ligands **1a** and **1b** were conveniently synthesized following the protocol developed by Odashima and co-workers [16]. The reaction of **1a** with corresponding ruthenium and osmium complexes [(*p*-cymene) $\text{MCl}_2$ ]<sub>2</sub> (where M = Ru, Os) in  $\text{CH}_2\text{Cl}_2$  under 1 atm of ethylene afforded complexes **2a-Cl<sub>2</sub>** and **3a-Cl<sub>2</sub>** as shown in Scheme 1. Purification of complexes by pass-

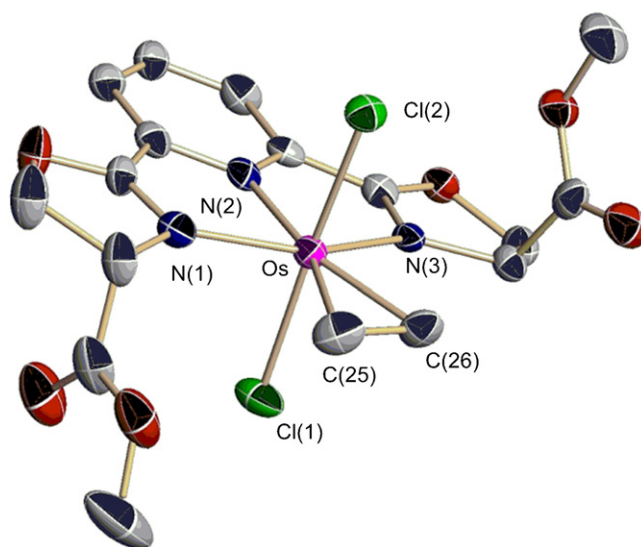


**Scheme 1.** Synthesis of complexes **2a-Cl<sub>2</sub>** and **3a-Cl<sub>2</sub>**.

ing through a silica gel plug with  $CH_2Cl_2/MeOH$  (1:1) afforded the corresponding (Pybox-CO<sub>2</sub>Me)M(II)Cl<sub>2</sub>(C<sub>2</sub>H<sub>4</sub>) complexes (M = Ru (**2a-Cl<sub>2</sub>**), Os (**3a-Cl<sub>2</sub>**)) in moderate yields (67.2% yield for **2a-Cl<sub>2</sub>**, 68.3% for **3a-Cl<sub>2</sub>**). In the case of complex **3a-Cl<sub>2</sub>**, both the *trans* and *cis*-chloride isomers were observed in ratio 2.9:1 respectively. Both the **2a-Cl<sub>2</sub>** and **3a-Cl<sub>2</sub>** have been fully characterized by NMR, mass spectrometry and elemental analysis. The solution <sup>1</sup>H and <sup>13</sup>C NMR of **2a-Cl<sub>2</sub>** and *trans*-**3a-Cl<sub>2</sub>** are consistent with a complex having C<sub>2</sub> symmetry, and consist of equivalent dihydrooxazole rings. The <sup>1</sup>H and <sup>13</sup>C NMR of *cis*-**3a-Cl<sub>2</sub>** is unsymmetrical and each dihydrooxazole ring is non equivalent.

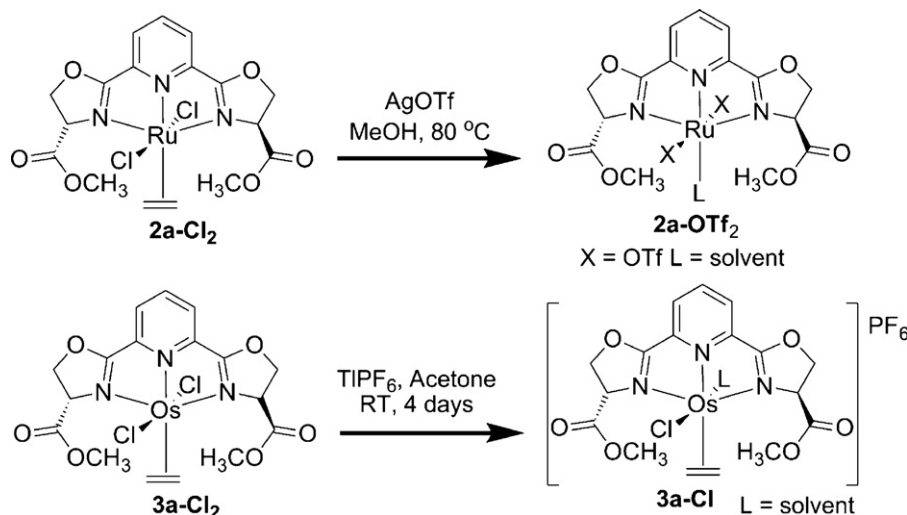
Complex *trans*-**3a-Cl<sub>2</sub>** was readily crystallized by vapor diffusion of pentane into  $CH_2Cl_2$  at room temperature, which was then analyzed by X-ray crystallography. An ORTEP drawing of the molecular structure is presented in Fig. 1. Metric parameters for complex *trans*-**3a-Cl<sub>2</sub>** can be found in the Supporting Information. The Os–N distances vary together and are the same within error in complex *trans*-**3a-Cl<sub>2</sub>**. The ethylene from **3a-Cl<sub>2</sub>** can be readily displaced. For example, when a sample of complex **3a-Cl<sub>2</sub>** was dissolved in NCCD<sub>3</sub> no reaction occurs until the sample is heated. Upon heating to 160 °C for 1 h, ethylene is displaced forming the acetonitrile adduct, (Pybox-CO<sub>2</sub>Me)OsCl<sub>2</sub>(NCC<sub>3</sub>H<sub>3</sub>). The formation of free ethylene was confirmed by sampling the headspace of the reaction mixture using GC–MS.

All attempts to make the corresponding osmium complexes of the aromatic Pybox ligand **1b**, had limited success. When **1b** and [(*p*-cymene)OsCl<sub>2</sub>]<sub>2</sub> were stirred in  $CH_2Cl_2$  with ethylene or *tert*-butylethylene, no reaction occurred and starting material was recovered. Following the standard procedures to make TerpyOsCl<sub>3</sub> complexes met with limited success. Heating **1b** and OsCl<sub>3</sub>·(H<sub>2</sub>O)<sub>3</sub> in various solvents such as MeOH, EtOH, DMF, and 2-methoxyethanol did not produce the desired

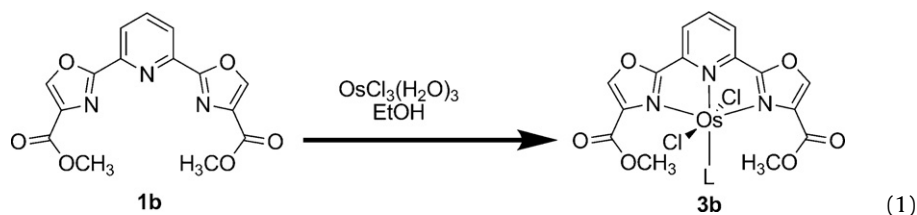


**Fig. 1.** ORTEP representation (30% probability level) of the molecular structure of complex *trans*-**3a-Cl<sub>2</sub>**. Co-crystallized methanol and water molecules and hydrogen atoms are removed for clarity.

(Pybox-CO<sub>2</sub>Me)Os(III)Cl<sub>3</sub> complex, and free ligand was recovered. However, depending on the solvent and conditions, small amounts of (Pybox-CO<sub>2</sub>R)Os(II)Cl<sub>2</sub>L (L = solvent, R = Me, Et) complexes (Eq. (1)) were obtained (<6% yield). When the reaction was performed in EtOH a mixture of the mixed esters was formed (R = R' = Et or Me; R = Me, R' = Et). Attempts to make the (Pybox-CO<sub>2</sub>Me)Os(III)Cl<sub>3</sub> complex with OsCl<sub>3</sub>Py<sub>3</sub> in EtOH or acetonitrile were also unsuccessful and starting material was recovered.

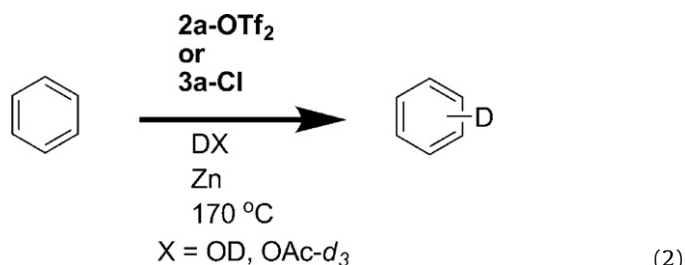


**Fig. 2.** Synthesis of complexes **2a-OTf<sub>2</sub>** and **3a-Cl**.



In order to generate a potential active catalyst we attempted to remove the chlorides with Tl and Ag salts (Fig. 2). The two chlorides were removed from the ruthenium complex by heating a solution of **2a-Cl<sub>2</sub>** with AgOTf in MeOH at 80 °C for 7 h in the dark. The resulting AgCl generated was removed by filtration, then the resultant species was precipitated from acetone with diethyl ether, yielding a new complex which has been assigned as the (Pybox-CO<sub>2</sub>Me)Ru(OTf)<sub>2</sub>L (**2a-OTf<sub>2</sub>**) complex (L = H<sub>2</sub>O, or acetone). MALDI-MS analysis supports the formation of such a complex and a peak at 732.87 (M–L)<sup>+</sup> was observed. The <sup>1</sup>H NMR of **2a-OTf<sub>2</sub>** in D<sub>2</sub>O showed several species, most likely a mixture of aquo, and hydroxyl complexes. However, when drops of 40 wt% KOD were added then only one species was observed. The sample is hygroscopic making an accurate elemental determination difficult; however elemental analysis of **2a-OTf<sub>2</sub>** is in the range of such a complex. Removing the chlorides from the osmium complex was much more difficult. When **3a-Cl<sub>2</sub>** is treated with TIPF<sub>6</sub> (2 equiv.) the formation of TlCl was observed, and a new species **3a-Cl** was observed by <sup>1</sup>H NMR. However, only 1 chloride was removed based on ESI-MS analysis, and **3a-Cl** is either the acetone or chloro bridge dinuclear complex. Using AgOTf or 5 equiv. of TIPF<sub>6</sub> in THF or CH<sub>2</sub>Cl<sub>2</sub> at ambient temperatures or refluxing conditions was unsuccessful.

With the Ru and Os Pybox complexes in hand we screened them for the H/D exchange reaction between benzene and DX (X = OD, OAc-*d*<sub>3</sub>) at temperatures up to 170 °C (Eq. (2)). We first screened **2a-OTf<sub>2</sub>** for H/D exchange in D<sub>2</sub>O. To make sure that MeOH generated from the hydrolysis of the ester had no deleterious effects we pretreated **2a-OTf<sub>2</sub>** in H<sub>2</sub>O with four equivalents of KOH, then removed the solvent. An 18.7 mM solution of **2a-OTf<sub>2</sub>** in D<sub>2</sub>O (1 mL) was heated in a 4 mL Schlenck bomb with 1 mL of benzene at 170 °C for 5.5 h and 17 h while rapidly stirring to ensure sufficient mass transfer. GC–MS analysis of the benzene layer at both times showed no significant H/D exchange (<0.5%). Under these protic conditions it is possible for the catalyst to be oxidized to Ru(III). Therefore we tried the reaction in the presence of excess Zn mesh, and after 5.5 h there was still no significant H/D exchange (<0.5%). When the reaction was done in 0.1 M KOD we saw no significant H/D exchange (<0.5%) after 5.5 h, but after 17 h ~6.4% (TON=98) of the benzene was deuterated (C<sub>6</sub>H<sub>5</sub>D = 3.6%, C<sub>6</sub>H<sub>4</sub>D<sub>2</sub> = 0.6%, C<sub>6</sub>H<sub>3</sub>D<sub>3</sub> = 0.3%, C<sub>6</sub>H<sub>2</sub>D<sub>4</sub> = 0.2%, C<sub>6</sub>HD<sub>5</sub> = 0.5%, C<sub>6</sub>D<sub>6</sub> = 1.2%).



Complex **2a-OTf<sub>2</sub>** showed some activity in acetic acid. A 13.7 mM solution of **2a-OTf<sub>2</sub>** in benzene/DOAc-*d*<sub>3</sub> (0.25:1 mL) heated at 170 °C for 5 h, had 2.7% (TON = 4.6) deuterium incorporation into benzene (C<sub>6</sub>H<sub>5</sub>D = 2.6%). After 17 h, there was only a slight increase, 6.6% (TON = 11.3) deuterium incorporation (C<sub>6</sub>H<sub>5</sub>D = 6.3%, C<sub>6</sub>H<sub>4</sub>D<sub>2</sub> = 0.3%). The catalyst was not stable under these conditions and a precipitate formed during the reaction. Addition of Zn

did not help the reaction: lower conversions were observed (3.1% deuterium incorporation), and more solid formed. Unfortunately, **2a-OTf<sub>2</sub>** is not an active catalyst for H/D exchange between benzene and DX (X = OD, OAc-*d*<sub>3</sub>).

Complexes **3a-Cl<sub>2</sub>** or **3a-Cl** were also tested, and found to be more active than **2a-OTf<sub>2</sub>**. When a 16.5 mM solution of **3a-Cl<sub>2</sub>** and 2 equiv. TIPF<sub>6</sub> in benzene/DOAc (0.2:1 mL) was heated at 160 °C for 5 h, catalytic deuterium incorporation (TON = 10.3) was observed although it was slow (TOF = 5.7 × 10<sup>−4</sup> s<sup>−1</sup>). After 5 h, there was 7.8% conversion (C<sub>6</sub>H<sub>5</sub>D 6.75%, and C<sub>6</sub>H<sub>4</sub>D<sub>2</sub> 0.8%). Control experiments without **3a-Cl<sub>2</sub>** show no H/D exchange. Similar results were obtained when the pretreated complex **3a-Cl** was used (5 h, 4.3% conversion, TON = 6.6). One potential reason for the low conversions under these conditions is protonation or oxidation of the Os(II) to Os(III), which most likely has a higher barrier for CH activation. When the reaction is carried out in the presence of Zn {to keep the Os as Os(II)} a much larger amount of H/D exchange was observed. Now 67% of the benzene has been deuterated: 39.2% C<sub>6</sub>H<sub>5</sub>D, 20.4% C<sub>6</sub>H<sub>4</sub>D<sub>2</sub>, 5.9% C<sub>6</sub>H<sub>3</sub>D<sub>3</sub>, 1.1% C<sub>6</sub>H<sub>2</sub>D<sub>4</sub> (TON = 181.9). Having found conditions at which **3a-Cl** is significantly active we now tested if we could observe H/D exchange between methane and DX (X = OAc-*d*<sub>3</sub>, and TFA). Unfortunately under these conditions no deuterium incorporation into methane was observed. **3a-Cl** is much less efficient a catalyst in D<sub>2</sub>O, and only trace amounts (<2%) of H/D exchange were observed at 170 °C for 4 h.

In order to gain insight into these catalytic systems, we studied their reaction mechanisms with density functional theory and the Poisson–Boltzmann polarizable continuum solvation model (M06//B3LYP flavor, see Section 2.2). For the Ru/PyBox system at pH = 7, we chose (dimethyl (S,S)-2,2′-pyridine-2,6-diyl)bis(4,5-dihydrooxazol-4-carboxylic acid) to represent the PyBox ligand, since **2a-OTf<sub>2</sub>** was pretreated in KOH to hydrolyze the ester. For the Ru/PyBox system at pH = 13, we chose (dimethyl (S,S)-2,2′-pyridine-2,6-diyl)bis(4,5-dihydrooxazol-4-acetate) to represent the PyBox ligand, assuming the two acidic protons are dissociated.

The calculated Gibbs free energy surfaces of benzene C–H activation by Ru/PyBox complexes at pH = 7 and pH = 13 are shown in Fig. 3. The calculations conclude that in both cases a hydroxide-bridged [(L)Ru(OH)(H<sub>2</sub>O)]<sub>2</sub> dimer (**Ru-1**) provides the resting state, in equilibrium with a deprotonated dimer [(L)Ru(OH)<sub>2</sub>]<sub>2</sub> (**Ru-2**), from which hydrolysis leads to the mononuclear Ru(OH)<sub>2</sub>(H<sub>2</sub>O) (**Ru-3**). The benzene C–H bond is activated through a substitution pathway, in which Ru–Ph and O–H bonds are formed in a concerted “2 + 2” rearrangement [33], leading to the formation of **Ru-4**, a Ru(Ph)(OH)(H<sub>2</sub>O) complex [34].

We found that the total benzene C–H activation barrier is 34.8 kcal/mol at pH = 13, while it is 45.6 kcal/mol at pH = 7. This suggests that this reaction is feasible at pH = 13 but thermally inaccessible at pH = 7, consistent with experimental results showing no reaction at pH = 7 but some reactivity at pH = 13. The disparate activation barriers are due to a resting state effect: dimerization of **Ru-3b** is much less favorable than that of **Ru-2b**. Due to the negatively charged carboxylate groups, **Ru-3b** must overcome a large electrostatic repulsion during dimerization. This is not the case for **Ru-3a**. In addition, the higher chemical potential of hydroxide at the higher pH drives the dissociation of the dimers according to Le Chatelier's Principle. This leads to a less stable resting

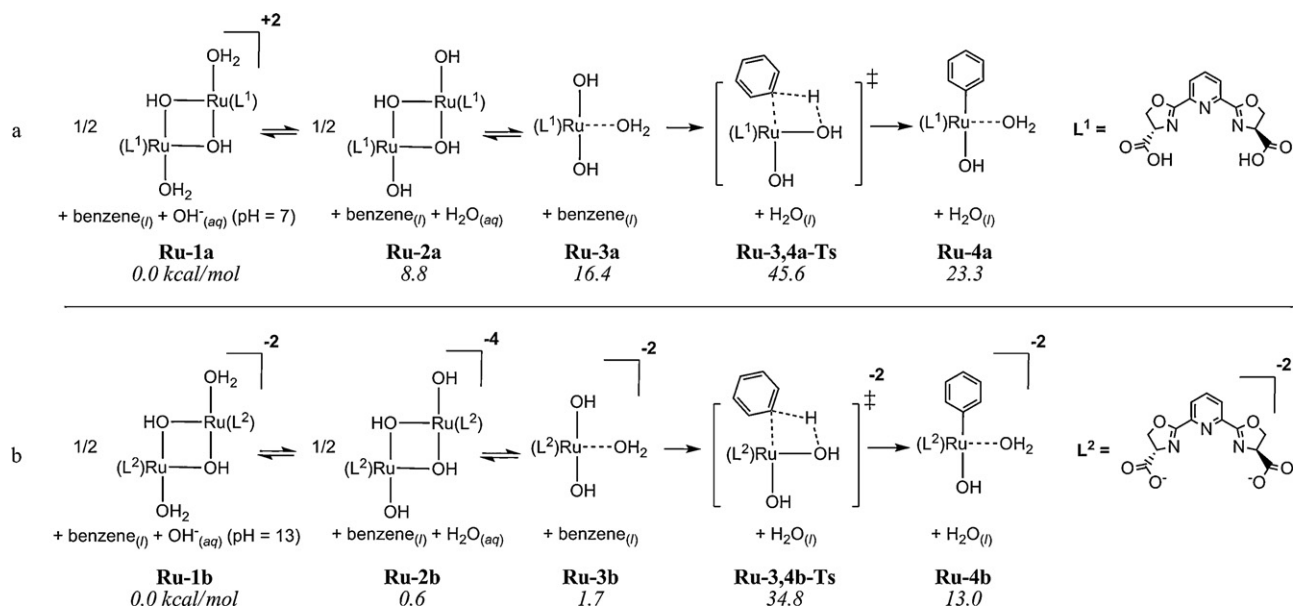


Fig. 3. Gibbs free energy surfaces (298 K in kcal/mol, including aqueous solvation) of benzene C–H activation by Ru/PyBox complexes at (a) pH = 7 and (b) pH = 13.

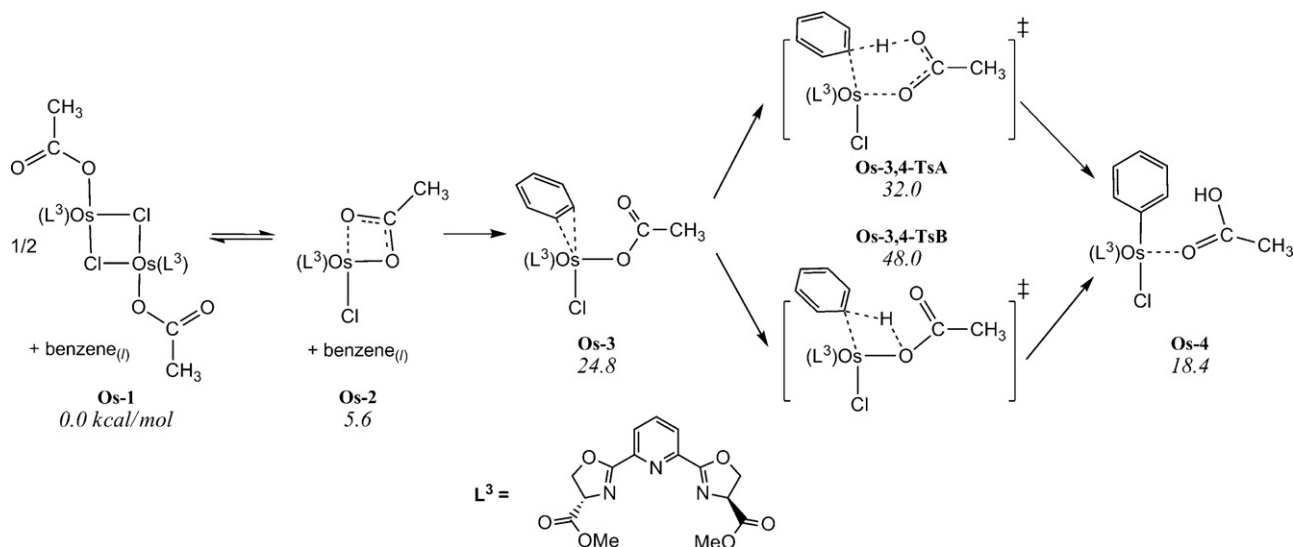


Fig. 4. Gibbs free energy surface (298 K in kcal/mol, including solvation by acetic acid) of benzene C–H activation by Os/PyBox complex.

state **Ru-1b** (1.7 kcal/mol downhill) and a smaller total barrier. Disregarding dimerization, the free energy difference  $\Delta G^\ddagger(\mathbf{Ru-3} \rightarrow \mathbf{Ru-3,4-Ts})$  is actually smaller for the neutral ligand, despite the observed reactivity. Interestingly, the negative charge of the deprotonated ligand affects the dimerization energy but not the  $pK_a$  of the bound aquo ligand in **Ru-1**. Hydroxide-bridged dinuclear ( $\text{Cp}^*\text{M}$ )<sub>2</sub>( $\mu\text{-OH}$ )<sub>3</sub><sup>+</sup> (M = Rh, Ir) complexes were found to result from deprotonation of monomeric  $\text{Cp}^*\text{M}(\text{H}_2\text{O})_3^{2+}$  [35]. We also found that the dinuclear [(NNC<sup>t-Bu</sup>)Ir(Ph)( $\mu\text{-OH}$ )]<sub>2</sub> resulted from Cl displacement from (NNC<sup>t-Bu</sup>)Ir(Ph)(Cl)Py rather than the monomeric (NNC<sup>t-Bu</sup>)Ir(Ph)(OH)Py despite the presence of pyridine [36].

For the Os/PyBox complex (Fig. 4), we found that the resting state is also a chloride-bridged [(L)Os(Cl)(OAc)]<sub>2</sub> dimer (**Os-1**). The formation of **Os-2** costs  $\Delta G = 5.6$  kcal/mol, and the coordination of benzene (**Os-3**) costs another 19.2 kcal/mol. Two transition states for CH cleavage were located. One has a six-membered ring structure [37] with an overall barrier of 32.0 kcal/mol (**Os-3,4-TsA**). The other has a four-membered geometry with a barrier of

48.0 kcal/mol (**Os-3,4-TsB**), indicating this pathway is thermodynamically inaccessible.

Our calculated results suggest 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). This is consistent with the observed relative turnover frequencies<sup>1</sup> of  $1.0 \times 10^{-2} \text{ s}^{-1}$  for **3a-Cl** at 160 °C and  $1.6 \times 10^{-3} \text{ s}^{-1}$  for **2a-OTf**<sub>2</sub> at pH = 13 and 170 °C, although the calculated barriers are each ~2.5 kcal/mol higher than a simple transition state theory analysis (i.e.,  $\text{TOF} = (kT/h) \exp(-\Delta G^\ddagger/kT)$ ) of the measured TOF would suggest. Computational and experimental studies directed to design more robust complexes for C–H activation with similar ancillary ligands are in progress.

<sup>1</sup> Turnover frequencies were estimated as (TON)/(reaction time), or 181.9/5 h =  $1.0 \times 10^{-2} \text{ s}^{-1}$  for **3a-Cl** and 98/17 h =  $1.6 \times 10^{-3} \text{ s}^{-1}$  for **2a-OTf**<sub>2</sub>.

#### 4. Concluding remarks

We have synthesized and characterized two new water soluble ruthenium and osmium (II) Pybox complexes **2a-Cl<sub>2</sub>** and **3a-Cl<sub>2</sub>**. In the case of **2a-Cl<sub>2</sub>** both chlorides were substituted with triflates (**2a-OTf<sub>2</sub>**) using AgOTf. Only one chloride (**3a-Cl**) could be removed in the case of **3a-Cl<sub>2</sub>**. Both of these complexes have been screened as catalysts for the H/D exchange reaction between benzene and DX (X = OD, OAc-*d*<sub>3</sub>). While **2a-OTf<sub>2</sub>** was an inefficient catalyst for deuterium incorporation into benzene, complex **3a-Cl** showed significant activity for the deuterium incorporation into benzene with DOAc-*d*<sub>3</sub> in the presence of zinc. DFT calculations find that a substitution mechanism is responsible for CH cleavage by both metals. Calculated activation barriers are dependent on the stability of dinuclear resting states, and thereby dependent on pH.

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#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2011.01.029.

#### References

- [1] (a) J. Atzrodt, V. Derrau, T. Fey, J. Zimmermann, *Angew. Chem. Int. Ed.* 46 (2007) 7744, and references therein; (b) S.R. Klei, J.T. Golden, T.D. Tilley, R.G. Bergman, *J. Am. Chem. Soc.* 124 (2002) 2092.
- [2] (a) B.L. Conley, W.J. Tenn III, K.J.H. Young, S. Ganesh, S. Meier, V. Ziatdinov, O. Mironov, J. Oxgaard, J. Gonzales, W.A. Goddard III, R.A. Periana, in: W.B. Tolman (Ed.), *Activation of Small Molecules*, Wiley-VCH, Weinheim, Germany, 2006, p. 235, and references therein; (b) K.J.H. Young, J. Oxgaard, D.H. Ess, S.K. Meier, T. Stewart, W.A. Goddard III, R.A. Periana, *Chem. Commun.* (2009) 3270.
- [3] (a) C. Jia, T. Kitamura, Y. Fujiwara, *Acc. Chem. Res.* 34 (2001) 633; (b) M. Muehlhofer, T. Strassner, W.A. Herrmann, *Angew. Chem. Int. Ed.* 41 (2002) 1745; (c) J.A. Labinger, J.E. Bercaw, *Nature* 417 (2002) 507; (d) R.H. Crabtree, *J. Chem. Soc. Dalton Trans.* (2001) 2437, and references therein.
- [4] (a) B. Hashiguchi, K.J.H. Young, M. Yousufuddin, W.A. Goddard III, R.A. Periana, *J. Am. Chem. Soc.* 132 (2010) 12542; (b) D.H. Ess, R.J. Nielsen, W.A. Goddard III, R.A. Periana, *J. Am. Chem. Soc.* 131 (2009) 11686; (c) S.K. Meier, K.J.H. Young, D.H. Ess, W.J. Tenn, J. Oxgaard, W.A. Goddard III, R.A. Periana, *Organometallics* 28 (2009) 5293; (d) V.R. Ziatdinov, J. Oxgaard, O.A. Mironov, K.J.H. Young, W.A. Goddard III, R.A. Periana, *J. Am. Chem. Soc.* 128 (2006) 7404, and references therein; (e) W.J. Tenn III, K.J.H. Young, J. Oxgaard, R.J. Nielsen, W.A. Goddard III, R.A. Periana, *Organometallics* 25 (2006) 5173.
- [5] (a) J.E. Bercaw, N. Hazari, J.A. Labinger, P.F. Oblad, *Angew. Chem. Int. Ed.* 47 (2008) 9941; (b) S.K. Hanson, D.M. Heinekey, K.I. Goldberg, *Organometallics* 27 (2008) 1454; (c) S.M. Kloeck, D.M. Heinekey, K.L. Goldberg, *Angew. Chem. Int. Ed.* 46 (2007) 4736; (d) G. Gerdes, P. Chen, *Organometallics* 23 (2004) 3031.
- [6] J.S. Johnson, D.A. Evans, *Acc. Chem. Res.* 33 (2000) 325.
- [7] For recent examples of early transition metal-Pybox catalysts; (a) T. Inagaki, L.T. Phong, A. Furuta, J. Ito, H. Nishiyama, *Chem. Eur. J.* 16 (2010) 3090; (b) M. Kawatsura, K. Kajita, S. Hayase, T. Itoh, *Synlett* (2010) 1243; (c) P.K. Singh, V.K. Singh, *Org. Lett.* 12 (2010) 80.
- [8] For recent examples involving lanthanide-Pybox catalysts; (a) G. Faita, M. Mella, M. Toscanini, G. Desimoni, *Tetrahedron* 66 (2010) 3024; (b) H. Suga, S. Higuchi, M. Ohtsuka, D. Ishimoto, T. Arikawa, Y. Hashimoto, S. Misawa, T. Tsuchida, A. Kakehi, T. Baba, *Tetrahedron* 66 (2010) 3070.
- [9] For a recent review, see: G. Desimoni, G. Faita, P. Quadrelli, *Chem. Rev.* 103 (2003) 3119.
- [10] K. Nomura, W. Sidokmai, Y. Imanishi, *Bull. Chem. Soc. Jpn.* 73 (2000) 599.
- [11] (a) S. Iwasa, A. Fakhruddin, H.S. Widagdo, H. Nishiyama, *Adv. Synth. Catal.* 347 (2005) 517; (b) S. Iwasa, K. Tajima, S. Tsumura, H. Nishiyama, *Tetrahedron Lett.* 42 (2001) 5897; (c) M.K. Tse, S. Bhor, M. Klawonn, G. Anilkumar, H. Jiao, C. Döbler, A. Spannenberg, W. Mägerlein, H. Hugl, M. Beller, *Chem. Eur. J.* 12 (2006) 1855; (d) M.K. Tse, C. Döbler, S. Bhor, M. Klawonn, W. Mägerlein, H. Hugl, M. Beller, *Angew. Chem. Int. Ed.* 43 (2004) 5255.
- [12] (a) H. Nishiyama, Y. Itoh, Y. Sugawara, H. Matsumoto, K. Aoki, K. Itoh, *Bull. Chem. Soc. Jpn.* 68 (1995) 1247; (b) H. Nishiyama, M. Kondo, T. Nakamura, K. Itoh, *Organometallics* 10 (1991) 500.
- [13] (a) H. Nishiyama, *Enantiomer* 4 (1999) 569; (b) H. Nishiyama, T. Shimada, H. Itoh, H. Sugiyama, Y. Motoyama, *Chem. Commun.* (1997) 1863; (c) S.B. Park, K. Murata, H. Matsumoto, H. Nishiyama, *Tetrahedron: Asymmetry* 6 (1995) 2487.
- [14] D. Cuervo, M.P. Gamasa, J. Gimeno, *Chem. Eur. J.* 10 (2004) 425.
- [15] J. Jankowska, J. Paradowska, B. Rakiel, J. Mlynarski, *J. Org. Chem.* 72 (2007) 2228.
- [16] Y. Hisamatsu, K. Hasada, F. Amano, Y. Tsubota, Y. Wasada-Tsutsui, N. Shirai, S.-I. Ikeda, K. Odashima, *Chem. Eur. J.* 12 (2006) 7733.
- [17] (a) D.-H. Lee, B.P. Patel, E. Clot, O. Eisenstein, R.H. Crabtree, *Chem. Commun.* (1999) 297; (b) R.H. Crabtree, J.A. Loch, K. Gruet, D.-H. Lee, C. Borgmann, *J. Organomet. Chem.* 600 (2000) 7–22.
- [18] (a) A.D. Becke, *Phys. Rev. A* 38 (1988) 3098; (b) A.D. Becke, *J. Chem. Phys.* 98 (1993) 5648; (c) C.T. Lee, W.T. Yang, R.G. Parr, *Phys. Rev. B* 37 (1988) 785.
- [19] (a) M.M. Franci, W.J. Pietro, W.J. Hehre, J.S. Binkley, M.S. Gordon, D.J. Defrees, J.A. Pople, *J. Chem. Phys.* 77 (1982) 3654; (b) W.J. Hehre, R. Ditchfie, J.A. Pople, *Chem. Phys.* 56 (1972) 2257.
- [20] P.J. Hay, W.R. Wadt, *J. Chem. Phys.* 82 (1985) 299.
- [21] (a) Y. Zhao, D.G. Truhlar, *Acc. Chem. Res.* 41 (2008) 157; (b) Y. Zhao, D.G. Truhlar, *Theor. Chem. Acc.* 120 (2008) 215.
- [22] (a) T. Clark, J. Chandrasekhar, G.W. Spitznagel, P.V. Schleyer, *J. Comput. Chem.* 4 (1983) 294; (b) R. Krishnan, J.S. Binkley, R. Seeger, J.A. Pople, *J. Chem. Phys.* 72 (1980) 650.
- [23] J.M.L. Martin, A. Sundermann, *J. Chem. Phys.* 114 (2001) 3408.
- [24] NIST Chemistry WebBook. <http://webbook.nist.gov/chemistry/> (retrieved 27.07.2010).
- [25] M.D. Tissandier, K.A. Cowen, W.Y. Feng, E. Gundlach, M.H. Cohen, A.D. Earhart, J.V. Coe, T.R. Tuttle, *J. Phys. Chem. A* 102 (1998) 7787.
- [26] S. Iwasa, H. Nakamura, H. Nishiyama, *Heterocycles* 52 (2000) 939.
- [27] A thick wall glass reactor sealed with a resealable PTFE valve.
- [28] J.A. Cabeza, P.M. Maitlis, *J. Chem. Soc. Dalton Trans.* (1985) 573.
- [29] K.J.H. Young, S.K. Meier, J.M. Gonzales, J. Oxgaard, W.A. Goddard III, R.A. Periana, *Organometallics* 25 (2006) 4734 (supporting information).
- [30] G.M. Sheldrick, SHELXTL, version 6.14, Bruker Analytical X-ray System Inc., Madison, WI, 1997.
- [31] R.H. Blessing, *Acta Crystallogr. A* 51 (1995) 33.
- [32] *Internal Tables for Crystallographers*, Vol. A, Space-Group Symmetry, D. Reidel Publishing Company, 1983, ISBN 90-277-r-1445-2.
- [33] (a) Y. Feng, M. Lail, N.A. Foley, T.B. Gunnoe, K.A. Barakat, T.R. Cundari, J.L. Petersen, *J. Am. Chem. Soc.* 128 (2006) 7982; (b) J. Oxgaard, W.J. Tenn, R.J. Nielsen, R.A. Periana, W.A. Goddard III, *Organometallics* 26 (2007) 1565; (c) W.J. Tenn, K.J.H. Young, G. Bhalla, J. Oxgaard, W.A. Goddard III, R.A. Periana, *J. Am. Chem. Soc.* 127 (2005) 14172.
- [34] Our attempt to optimize a stable ruthenium–benzene adduct which might precede CH activation led only to a 5-coordinate ruthenium complex and liberated benzene, suggesting no coordination barrier exists.
- [35] (a) A. Nutton, P.M. Bailey, P.M. Maitlis, *J. Chem. Soc. Dalton Trans.* (1981) 1997; (b) S. Cayemittes, T. Poth, M.J. Fernandez, P.G. Lye, M. Becker, H. Elias, A.E. Merbach, *Inorg. Chem.* 38 (1999) 4309.
- [36] S.K. Meier, K.J.H. Young, D.H. Ess, W.J. Tenn III, J. Oxgaard, W.A. Goddard III, R.A. Periana, *Organometallics* 28 (2009) 5293.
- [37] (a) C.J. Jones, D. Taube, V.R. Ziatdinov, R.A. Periana, R.J. Nielsen, J. Oxgaard, W.A. Goddard, *Angew. Chem. Int. Ed.* 43 (2004) 4626; (b) D.L. Davies, S.M.A. Donald, O. Al-Duaij, S.A. Macgregor, M. Palleth, *J. Am. Chem. Soc.* 128 (2006) 4210; (c) D.L. Davies, S.M.A. Donald, S.A. Macgregor, *J. Am. Chem. Soc.* 127 (2005) 13754; (d) D.H. Ess, S.M. Bischof, J. Oxgaard, R.A. Periana, W.A. Goddard III, *Organometallics* 27 (2008) 6440.