# Synthesis of Tris(4,7-diphenyl-1,10-phenanthroline)ruthenium(II) Complexes Possessing a Linker Arm for Use in Sol-gel-based Optical Oxygen Sensor

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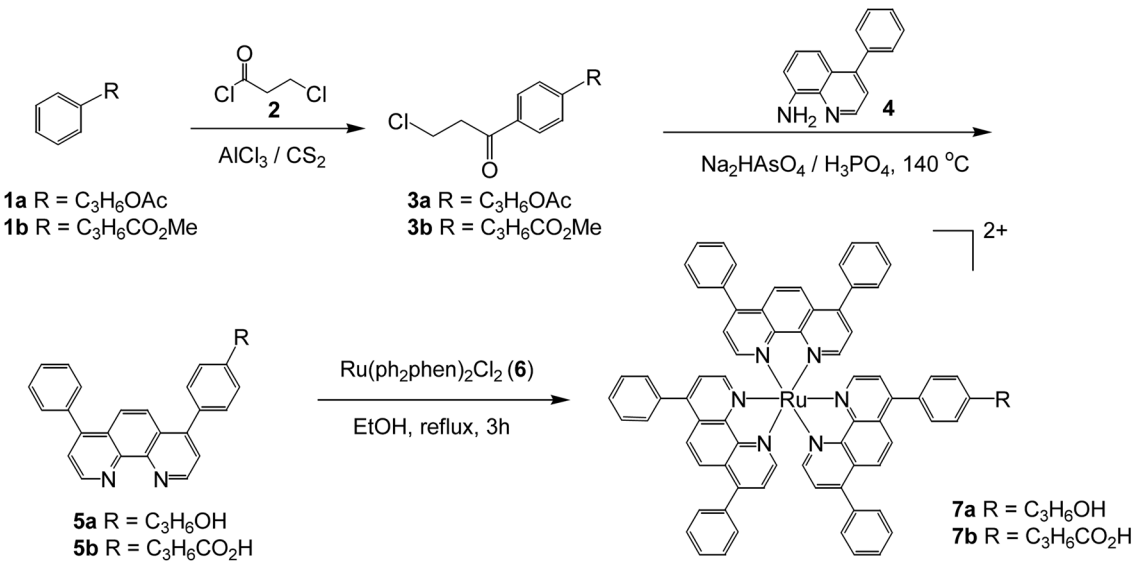
In recent years, there has been considerable interest in the development of optical sensors for oxygen detection because oxygen measurements are widely applied to biological,[1] environmental,[2] and industrial[3] areas.

Ruthenium(II) complexes are attractive fluorophores for use in fluorescence-based oxygen sensors because of their high photochemical stability, high molar absorptivity, long lifetime derived from the metal to ligand charge transfer (MLCT) excited states, and large Stokes shift.[4-7] The immobilization of Ru(II) complexes in sol-gel matrices has been recently investigated for the development of optical sensors.[8-12] Although these developments generally employ the impregnation or doping of dye molecules into sol-gels, such methods could cause leaching of dye molecules from the host sol-gel matrix to the analyte solution during liquid-phase sensing and could eventually reduce sensor lifetime. To circumvent the problem of leaching, an alternative method is the covalent immobilization of dye molecules on the sol-gel matrix. Therefore, to develop a stable, oxygen-sensing material without the leaching problem, we investigated the formation of covalent bonds between fluorophores and sol-gel precursors. Herein, we report the synthesis of Ru(II) complexes possessing a linker arm which is a functional group for forming a covalent linkage with an appropriate silicate precursor.

Tris(4,7-diphenyl-1,10-phenanthroline)ruthenium(II) complex is the fluorophore of choice in this work since it is a well-known fluorescent dye quenched dynamically by oxygen.[9]

To synthesize the dye molecule **7** which enables covalent binding with a silicate precursor, we designed ligands, comprising phenanthroline derivatives having either a hydroxypropyl (**5a**) or carboxypropyl group (**5b**), which are readily coupled with reactive silicate precursors such as 3-(triethoxysilyl)propyl isocyanate or (3-chloropropyl)triethoxysilane (Scheme 1). Thus, phenyl derivatives (**1a** and **1b**), the functional groups of which were protected with acetyl or methyl ester groups, were reacted with 3-chloropropionyl chloride (**2**) under the traditional Friedel-Craft's acylation reaction conditions to afford 3-chloro-1-propanone derivatives (**3a** and **3b**) in high yields. The protective groups survived under the acylation reaction conditions. The preparation of two different ligands (**5a** and **5b**) was then achieved *via* an oxidative cyclization of aminoquinoline[10] (**4**) with two different 3-chloro-1-propanone derivatives (**3a** and **3b**) in the presence of sodium arsenate in phosphoric acid at 140 °C to afford phenanthroline derivatives **5a** and **5b**, respectively. The acetyl group of **3a** was removed and the ester group of **3b** was also transformed to free acid by acidic




**Scheme 1**

hydrolysis during this reaction. Structural confirmation of ligand **5** was supported by the appearance of the appropriate peaks for the phenanthroline moiety in $^1$H and $^{13}$C NMR spectroscopy as well as the molecular ion peaks (ESI-MS) at *m/z* 391.18 [(M + H) $^+$] for **5a** and at *m/z* 419.1 [(M + H)$^+$] for **5b**. Ligand **5** was then reacted with *bis*(4,7-diphenyl-1,10-phenantroline)ruthenium(II) chloride[11] [Ru(ph$_2$phen)$_2$Cl$_2$] (**6**) in boiling ethanol to afford the crude red crystalline ruthenium complex **7**, which was successfully purified by column chromatography by eluting with a 20 : 1 : 1 mixture of acetonitrile/saturated aqueous potassium nitrate/water on silica gel. The structure of complex **7** was identified by the MALDI-TOF MS peaks at *m/z* 1156.28 [(M-2NO$_3$)$^{2+}$] for **7a** and at *m/z* 2285.34 [(M-2PF$_6$)$^{2+}$] for **7b**, as well as by the newly appeared resonance peaks ($^1$H and $^{13}$C NMR) based on the ligand, 4,7-diphenyl-1,10-phenantroline. Further corroboration for the complexation was provided by the expected upfield shifts ($^1$H NMR) of the resonance assigned to the 2,9- and 3,8-phenanthroline protons upon complexation (id., in case of **7a**, from $\delta$ = 9.24 and 7.83 ppm to $\delta$ = 8.59 and 7.83 ppm, respectively).

The 2D fluorescence spectra of **7** in methanol solution are shown in Figure 1. Like tris(4,7-diphenyl-1,10-phenanthroline)ruthenium dichloride [(Ru(ph$_2$phen)$_3$Cl$_2$],[12] both **7a** and **7b** display a strong fluorescence emission at 600 nm with exitation wavelenth of 480 nm, which indicates that **7** will be a good oxygen sensor equal to (Ru(ph$_2$phen)$_3$Cl$_2$.

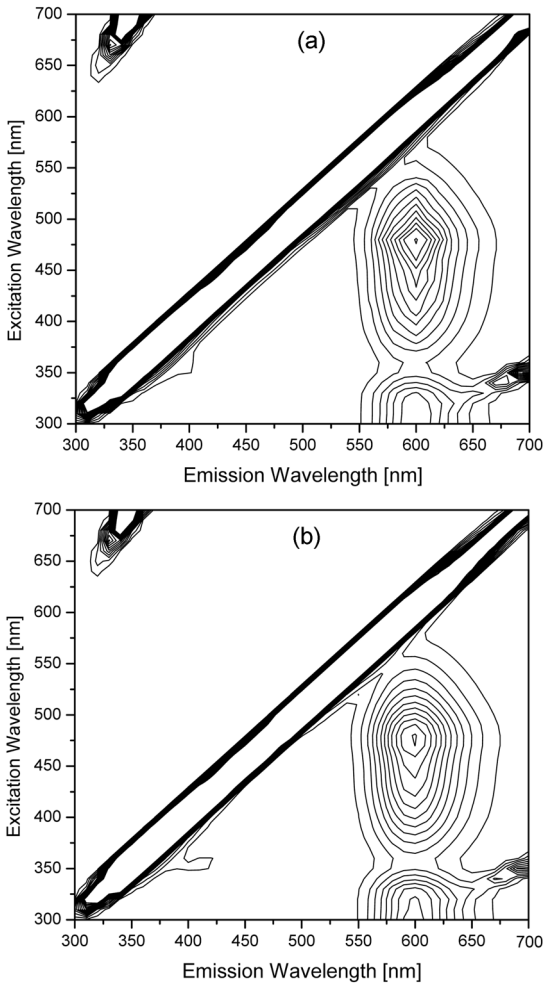



**Figure 1**. 2D fluorescence spectra of (a) complex **7a** and (b) complex **7b** in MeOH ($2.5 \times 10^{-7}$ M) at 25 °C.

In summary, for the development of optical oxygen sensors able to form a covalent bond with a silicate precursor, a tris(4,7-diphenyl-1,10-phenanthroline)ruthenium(II) complex **7** possessing a linker arm was synthesized from the corresponding phenanthroline derivative **5**, which was readily prepared by the oxidative cyclization of aminoquinoline **4** with 3-chloro-1-propanone derivative **3**. The structure of **7** was characterized based on the $^1$H and $^{13}$C NMR, as well as the MS spectral data. The development of optical oxygen sensing materials based on the covalent immobilization of complex **7** in sol-gels is in progress and the results will be published soon.

## Experimental Section

The melting points were determined with a MEL-TEMP capillary melting point apparatus and are reported uncorrected. $^1$H and $^{13}$C NMR spectra were recorded at 300 and 71 MHz, respectively, on a Bruker ARX-R300 spectrometer and were obtained in $CDCl_3$. IR spectra were recorded on a Shimadzu FTIR-8300 spectrophotometer. Mass spectral data were obtained on either a Jeol JMS-HX110 high resolution tandem mass spectrometer (ESI-MS) or a Voyager DE-STR proteomics analyzer (MALDI-TOF). Fluorescence measurements were performed with a Hitachi F-4500 fluorescence spectrophotometer. All regents were obtained from Aldrich Chemical Co. and used without further purification. THF was dried by refluxing with benzophenone/Na under $N_2$ atmosphere. 4-Phenylquinolin-8-ylamine (**4**) and bis(4,7-diphenyl-1,10-phenantroline)ruthenium(II) chloride [Ru(ph$_2$phen)$_2$Cl$_2$] (**6**) were prepared according to the reported procedure.[13,14]

**3-[4-(3-Chloropropionyl)phenyl]propyl acetate (3a).** To a stirred mixture of 3-chloropropionyl chloride (2.35 g, 18.5 mmol) and $AlCl_3$ (8.3 g, 62.3 mmol) in $CS_2$ (8 mL), 3-phenylpropyl acetate **2a** (3 g, 16.83 mmol) was slowly added for 5 min at 0 °C, after which the mixture was stirred for 1 h at 25 °C and for a further 1 h at 40 °C. After cooling to 25 °C, the reaction mixture was poured into a stirred mixture of ice water (100 mL) and $Et_2O$ (50 mL). The organic layer was separated, washed with water (100 mL × 2) and saturated aqueous $NaHCO_3$ (100 mL × 2), and then dried ($MgSO_4$). The organic mixture was concentrated in vacuo to give ester **3** (3.87 g, 86%) as a clear liquid. $^1$H NMR $\delta$: 7.88 (d, 2H, *J* = 8.13 Hz, Ar*H*), 7.29 (d, 2H, *J* = 8.04 Hz, Ar*H*), 4.08 (t, 2H, *J* = 6.24 Hz, ClC*H*$_2$CH$_2$), 3.92 (t, 2H, *J* = 6.54 Hz, C*H*$_2$O), 3.44 (t, 2H, *J* = 6.48 Hz ClCH$_2$C*H*$_2$), 2.76 (t, 2H, *J* = 7.53 Hz, C*H*$_2$Ar), 2.03 (s, 3H, COC*H*$_3$). 1.98 (m, 2H, CH$_2$C*H*$_2$CH$_2$). $^{13}$C NMR $\delta$: 196.2, 170.9, 147.5, 134.4 (Ar*C*CO), 128.72 (2,6-Ar*C*), 128.4 (3,5-Ar*C*), 63.4 (CH$_2$CH$_2$*C*H$_2$O), 41.1 (ClCH$_2$*C*H$_2$), 38.7 (Cl*C*H$_2$CH$_2$), 32.1 (*C*H$_2$CH$_2$CH$_2$O), 29.7 (CH$_2$*C*H$_2$CH$_2$O), 20.8 (*C*H$_3$). ESI-MS for $C_{14}H_{17}ClO_3$: calcd 268.0, found 269.1 [M + H] $^+$.

**Methyl 4-[4-(3-chloropropionyl)phenyl]butyrate (3b).** was prepared in 94% yield (2.84g) from 3-chloropropionyl chloride (1.57 g, 12.3 mmol), methyl 4-phenylbutyrate (2 g, 11.2 mmol) and $AlCl_3$ (5.51 g, 41.7 mmol) in $CS_2$ (5 mL) following the same method as that of **3a**. $^1$H NMR $\delta$: 7.89 (d, 2H, $J$ = 8.24 Hz, Ar*H*), 7.29 (d, 2H, $J$ = 8.24 Hz , Ar*H*), 3.90 (t, 2H, $J$ = 6.84 Hz, ClC*H*$_2$CH$_2$), 3.65 (s, 3H, COC*H*$_3$), 3.42 (t, 2H, $J$ = 6.48 Hz ClCH$_2$C*H*$_2$), 2.70 (t, 2H, $J$ = 7.32 Hz, C*H*$_2$Ar), 2.32 (t, 2H, $J$ = 7.38 Hz, C*H*$_2$CH$_2$Ar), 1.96 (m, 2H, CH$_2$C*H*$_2$-CH$_2$), $^{13}$C NMR $\delta$: 196.2 (ClCH$_2$CH$_2$*C*O), 173.5 (*C*O$_2$), 147.7 (Ar*C*CH$_2$), 134.5 (Ar*C*CO), 128.8 (2,6-Ar*C*), 128.3 (3,5-Ar*C*), 51.5 (*C*H$_3$), 41.1 (ClCH$_2$*C*H$_2$), 38.7 (Cl*C*H$_2$), 35.0 (*C*H$_2$CH$_2$-CH$_2$CO), 33.2 (CH$_2$CH$_2$*C*H$_2$CO), 26.0 (CH$_2$*C*H$_2$CH$_2$O). ESI-MS for $C_{14}H_{17}ClO_3$: calcd 268.0, found 269.1 $[M + H]^+$.

**3-[4-(7-Phenyl-1,10-phenantrolin-4-yl)phenyl]propan-1-ol: ph$_2$phen$C_3H_6$OH (5a).** To a stirred solution of 4-phenylquinolin-8-ylamine **4** (300 mg, 1.36 mmol) and $Na_2HAsO_4{\cdot}7H_2O$ (850 mg, 2.72 mmol) in 85% $H_3PO_4$ (5 mL) at 100 °C, ester **3a** (512 mg, 7.91 mmol) was slowly added. After addition, the temperature was raised to 140 °C and maintained for 2 h. The reaction mixture was then cooled, poured into ice-water, and neutralized with 30% aqueous KOH. The resulting mixture was extracted with $CH_2Cl_2$ and the extract was dried ($MgSO_4$). After concentration in vacuo, the crude product was chromatographed (basic $Al_2O_3$) by eluting with a 5:95 mixture of MeOH/$CHCl_3$ to afford alcohol **5** (485 mg, 65%) as a brown oil. $^1$H NMR $\delta$: 9.24 (m, 2H, 2,9-$H_{phenan}$), 7.89 (m, 2H, 5,6-$H_{phenan}$), 7.58 (m, 2H, 3,8-$H_{phenan}$), 7.52-7.36 (m, 9H, phenyl), 3.76 (t, 2H, $J$ = 6.42 Hz, C*H*$_2$OH), 2.84 (t, 2H, $J$ = 7.38 Hz, C*H*$_2$-CH$_2$CH$_2$OH), 2.19 (bs, 1H, O*H*), 1.99 (m, 2H, C*H*$_2$CH$_2$OH). $^{13}$C NMR $\delta$: 149.6, 148.67, 148.62, 146.43, 146.41, 142.54, 138.80, 135.30, 129.70, 129.62, 128.72, 128.6, 128.52, 126.47, 126.40, 124.14, 123.95, 123.54, 62.07, 34.08, 31.83. ESI-MS for $C_{27}H_{22}N_2O$: calcd 390.17, found 391.18 $[M + H]^+$.

**4-[4-(7-Phenyl-1,10-phenantrolin-4-yl)phenyl]butyric acid (5b).** was prepared from 4-phenylquinolin-8-ylamine **4** (750 mg, 3.4 mmol), eater **3b** (1.28 g, 4.8 mmol), and $Na_2HAsO_4{\cdot}7H_2O$ (2.12 g, 6.8 mmol) in 85% $H_3PO_4$ (5 mL) following the same method as that of **5a**. Crude product was recrystallized from a mixture of benzene and $Et_2O$ to give acid **5b** (860 mg, 60%) as a white solid; mp 194-196 °C. $^1$H NMR $\delta$: 9.30 (m, 2H, 2,9-$H_{phenan}$), 7.89 (m, 2H, 5,6-$H_{phenan}$), 7.63 (m, 2H, 3,8-$H_{phenan}$), 7.52-7.34 (m, 9H, phenyl), 6.61 (bs, 1H, CO$_2$*H*), 2.79 (t, 2H, $J$ = 7.32 Hz, C*H*$_2$CH$_2$CH$_2$CO$_2$H), 2.46 (t, 2H, $J$ = 7.41 Hz, C*H*$_2$CO$_2$H), 2.06 (m, 2H, C*H*$_2$CH$_2$-CO$_2$H). $^{13}$C NMR $\delta$: 177.8, 149.4, 149.3, 149.29, 149.20, 145.6, 142.2, 137.6, 135.3, 129.7, 129.6, 128.8, 128.7, 126.6, 126.5, 124.2, 124.1, 123.7, 34.8, 33.2, 26.2. ESI-MS for $C_{27}H_{22}N_2O$: calcd 418.1, found 419.1 $[M + H]^+$.

**Bis(4,7-diphenyl-1,10-phenantroline){3-[4-(7-phenyl-1,10-phenantrolin-4-yl)phenyl]propan-1-ol}ruthenium(II) hexafluorophosphate (7a).** Alcohol **5a** (118 mg, 0.30 mmol) and complex **6** (220 mg, 0.25 mmol) were dissolved in EtOH (10 mL) and refluxed for 3 h under $N_2$ atmosphere. After cooling to 25 °C, the reaction mixture was concentrated in vacuo, chromatographed ($SiO_2$) by eluting with a 20 : 1 : 1 mixture of CHCN/saturated aqueous $KNO_3$/$H_2O$, and then treated with methanolic $NH_4PF_6$ to afford complex **7** (257 mg, 71%) as a red solid; mp > 300 °C. $^1$H NMR $\delta$: 8.59 (bs, 6H, 2,9-$H_{phenan}$), 8.19 (s, 6H, 5,6-$H_{phenan}$), 7.83 (bs, 6H, 3,8-$H_{phenan}$), 7.52-7.36 (m, 27H, ArC*H*), 7.36 (m, 2H, ArC*H*), 3.68 (t, 2H, $J$ = 6.39 Hz, C*H*$_2$OH), 2.80 (t, 2H, $J$ = 7.29 Hz, C*H*$_2$CH$_2$CH$_2$OH), 1.94 (m, 2H, C*H*$_2$CH$_2$OH). $^{13}$C NMR $\delta$: 153.45, 148.83, 148.25, 143.84, 135.59, 133.09, 130.01, 129.57, 129.15, 129,. 128.62, 127.03, 126.05, 125.92, 125.80, 61.94, 33.97, 31.43. MALDI-TOF MS for $C_{75}H_{54}F_{12}N_8O_7P_2Ru$: calcd 1446.27, found 1156.28 $[M\text{-}2PF_6]^{2+}$.

**Bis(4,7-diphenyl-1,10-phenantroline){4-[4-(7-phenyl-1,10-phenantrolin-4-yl)phenyl]butyric acid}ruthenium(II) hexafluorophosphate (7b).** was prepared from acid **5b** (158 mg, 0.38 mmol) and complex **6** (248 mg, 0.29 mmol) as described in the preparation of **7a**. After column chromatography, the product was treated with methanolic $NH_4PF_6$ to afford **7b** (312 mg, 73%) as a red solid; mp > 280 °C. $^1$H NMR $\delta$: 8.41 (bd, 6H, 2,9-$H_{phenan}$), 8.33 (s, 6H, 5,6-$H_{phenan}$), 7.80-7.54 (m, 35H, Ar), 2.87 (t, 2H, $J$ = 7.23 Hz, C*H*$_2$CH$_2$-CH$_2$CO$_2$H), 2.45 (t, 2H, $J$ = 7.38 Hz, C*H*$_2$CO$_2$H), 2.05 (m, 2H, C*H*$_2$CH$_2$CO$_2$H). $^{13}$C NMR $\delta$: 173.4, 153.3, 149.9, 149.4, 145.1, 136.6, 130.8, 130.7, 130.5, 130.1, 130.0, 129.8, 126.9, 34.5, 33.4, 26.3. MALDI-TOF MS for $C_{75}H_{54}F_{12}N_8O_7P_2Ru$: calcd 1474.26, found 1185.34 $[M\text{-}2PF_6]^{2+}$.

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