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The synthesis and characterization of $Re(CO)_3$ pyca-anthraquinone conjugates

Briana R. Schrage [a], Richard S. Herrick [b], Christopher J. Ziegler [a, *]

[a] Department of Chemistry, University of Akron, Akron, OH, 44312-3601, USA
[b] Department of Chemistry, College of the Holy Cross, 1 College St, Worcester, MA, 01610, USA

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ABSTRACT

Three rhenium carbonyl anthraquinone species have been synthesized (compounds **1**–**3**) using a one-pot methodology. The synthesis involves use of pyridine-2-carboxyaldehyde, which reacts with primary amines and $Re(CO)_5X$ to form a metal bound diamine. Reactions with $Re(CO)_5Cl$ and $Re(CO)_5Br$ afford compounds **1** and **2** respectively, where the anthraquinone unit is pendant to the pyridine aldimine unit. Compound **3** can be produced upon replacement of the halide in **1** and **3** with pyridine. These three complexes have been fully characterized, including by single crystal X-ray diffraction. Compounds **1**–**3** exhibit metal-to-ligand charge transfer bands in their UV–visible spectra. Additionally, the electrochemical behaviour of **1**–**3** has been investigated, and all three compounds show positive shifts in their reduction potentials relative to aminoanthraquinone.

1. Introduction

Metallointercalators are a well-known class of inorganic compounds that exhibit the ability to interact non-covalently with DNA via intercalation between base pairs. First investigated nearly four decades ago by Lippard and Barton, metallointercalators are often either planar in structure, such as d^8 Pt(II) complexes, or octahedral species with pendant planar aromatic groups, such as the Ru(II) $(diimine)_3$ class of compounds. Additionally, this chemistry can be imparted on a metal complex via covalent linkage to an intercalating organic group, such as a π-conjugated polycyclic unit [1,2]. Previously, one way to accomplish this is via π expansion of a diimine ligand such that the linear portion of the chelate extends significantly beyond the initial coordination sphere of the metal complex [3–11].

Anthraquinones have long been used as DNA intercalating moieties. Schuster and co-workers have synthesized many examples of organic compounds that employ the anthraquinone moiety to target DNA [12–17]. Anthraquinones have also been previously incorporated into metal binding ligands to generate metallointercalators, such as in the systems developed by Turro and co-workers [18–25]. 2-Aminoanthraquinione, shown in Scheme 1, is a convenient commercially available starting material for the functionalization of this organic unit, and we have used similar primary amines in one-pot syntheses to produce $Re(CO)_3$ complexes. Pyridine-2-carboxyaldehyde reacts with $Re(CO)_5X$ complexes either sequentially or in one step to produce pyridine-2-carboxaldimine (pyca) compounds where the primary amine is incorporated into the metal binding diimine unit. Previously, we have used this synthetic strategy to produce amino acid conjugates, pH sensitive phenolic compounds, modular ferrocene compounds, azobenzene conjugates, and $Re(CO)_3$ organometallic polymers [26–31].

In this report, we present the synthesis of a series of three Re(pyca) complexes where an anthraquinone unit has been placed pendant to the diimine unit (Scheme 1). Re(pyca) anthraquinones **1** and **2** can be produced in one-step from commercially available reagents, and the halide can be removed by metathesis using Ag(I) and replaced with a pyridine, yielding the cationic complex **3**. Compounds **1**–**3** have been fully characterized, including by single crystal X-ray diffraction. These compounds have been synthesized as a first step in designing $Re(CO)_3$ intercalators that can be readily produced via one-pot synthetic methodologies.

2. Materials and methods

All reagents and starting materials were purchased from commercial vendors and used without further purification. Deuterated solvents were purchased from Cambridge Isotope Laboratories and

* Corresponding author.
E-mail address: ziegler@uakron.edu (C.J. Ziegler).

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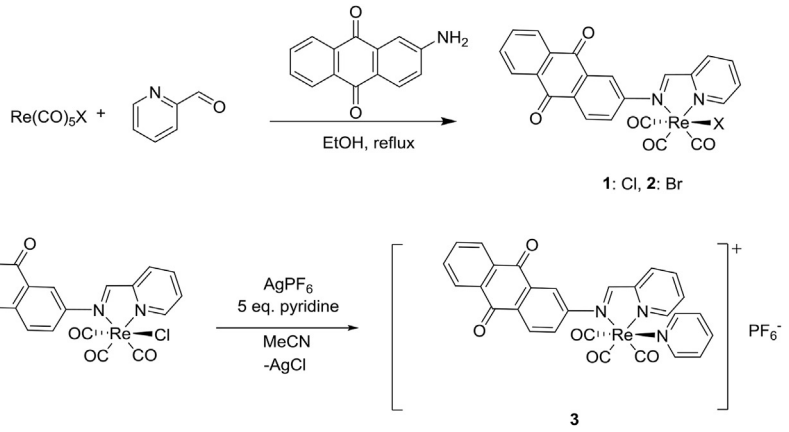

Scheme 1. Syntheses of compounds **1**–**3**.

used as received.

^{1}H and ^{13}C NMR spectra were recorded on a 500 MHz spectrometer and chemical shifts were given in ppm relative to residual solvent. High resolution mass spectrometry experiments were performed on a Bruker MicroTOF-III instrument. Infrared spectra were collected on Thermo Scientific Nicolet iS5 instrument which was equipped with an iD5 ATR. UV–visible spectra were recorded using a Hitachi U-3010 spectrometer.

2.1. X-ray data collection and structure determination

X-ray intensity data were measured on a Bruker CCD-based diffractometer with dual Cu/Mo ImuS microfocus optics (Cu Kα radiation, λ = 1.54178 Å, Mo Kα radiation, λ = 0.71073 Å). Crystals were mounted on a cryoloop using Paratone oil and placed under a steam of nitrogen at 100 K (Oxford Cryosystems). The detector was placed at a distance of 5.00 cm from the crystal. The data were corrected for absorption with the SADABS program. The structures were refined using the Bruker SHELXTL Software Package (Version 6.1), and were solved using direct methods until the final anisotropic full-matrix, least squares refinement of F2 converged. CCDC 1867176-1867178 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/structures.

2.2. Cyclic voltammetry

Electrochemistry measurements were conducted using a CHI 820D potentiostat in a standard three-electrode configuration. Platinum wire was used as the counter electrode. The working electrode used was a 2 mm diameter platinum disk. A nonaqueous Ag/Ag^{+} reference electrode was used by immersing silver wire in a degassed dimethylformamide (DMF) solution of 0.01 M $AgNO_3$/0.1 M tetrabutylammonium hexafluorophosphate ($TBAPF_6$). All potentials were referenced to the ferrocene/ferrocenium couple. The concentration of analyte was 1.0 mM, and the supporting electrolyte was 0.1 M $TBAPF_6$ dissolved in DMF.

2.3. Syntheses of compounds 1-3

Synthesis of 1 and 2. For the synthesis of **1** and **2**, a one-pot method was employed. The synthesis of **2** is the same as **1** except $Re(CO)_5Br$ (56.05 mg, 0.138 mmol) was used. To synthesize **1**, $Re(CO)_5Cl$ (50.00 mg, 0.138 mmol), and one equivalent of 2-aminoanthraquinone (30.9 mg, 0.138 mmol) were combined in a round bottom flask with 7.0 mL of ethanol. One equivalent of pyridine-2-carboxaldehyde (0.013 mL, 0.138 mmol) was added to the ethanolic mixture and refluxed overnight. After cooling to room temperature, the solution was filtered and washed with hot ethanol to afford an orange solid for **1**, and red solid for **2**. Crystals of **1** and **2** suitable for X-ray diffraction were grown by vapor diffusion of water into a DMSO solution.

1:Yield: 55 mg (64%). IR (**C≡O** stretch, cm^{-1}): 1893 (s), 1945 (s), 2017 (vs). IR (C═O stretch, cm^{-1}): 1675 (m). ESI MS (positive mode) calcd $C_{23}H_{12}N_2O_5Re$ 583.0276 *m/z*, found 583.0353. ^{1}H NMR (500 MHz, d_6 - DMSO): δ = 9.56 (s, 1H, H–C═N), 9.12 (d, ^{3}J = 5.4 Hz, 1H, H on py), 8.46–8.37 (m, 4H, H on anthraquinone), 8.26 (m, 2H, H on py and anthraquinone), 8.09 (m, 1H, H on anthraquinone), 7.97 (m, 2H, H on py and anthraquinone), 7.91 (m, 1H on py). ^{13}C NMR (125 MHz, d_6 – DMSO): δ = 187.4 (C═O), 181.9 (C≡O), 181.7 (C≡O), 172.3, 154.9, 154.6, 153.3, 140.7, 134.9, 134.7, 134.5, 133.2, 133.0, 131.3, 130.5, 128.9, 128.3, 127.0, 120.4.

2: Yield: 61 mg (67%). IR (**C≡O** stretch, cm^{-1}): 1893 (s), 1943 (s), 2018 (vs). IR (C═O stretch, cm^{-1}): 1673 (m). ESI MS (positive mode) calcd $C_{23}H_{12}N_2O_5ReBr$ 661.9459 *m/z*, found 661.9447. ^{1}H NMR (500 MHz, d_6 - DMSO): δ = 9.54 (s, 1H, H–C═N), 9.15 (d, ^{3}J = 4.9 Hz, 1H, H on py), 8.46–8.39 (m, 4H, H on anthraquinone, 8.27 (m, 4H, H on py and anthraquinone), 8.11 (m, 1H, H on anthraquinone), 7.98 (m, 2H, H on py and anthraquinone), 7.90 (m, 1H, H on py). ^{13}C NMR (125 MHz, d_6 – DMSO): δ = 186.6 (C═O), 181.6 (C≡O), 172.1, 154.6, 153.4, 140.5, 134.8, 134.6, 134.4, 133.1, 132.9, 131.2, 130.2, 128.8, 128.2, 126.9, 120.3.

Synthesis of 3. This reaction can be carried out with either **1** or **2**; the procedure with **1** follows. Compound **1** (50 mg, 0.081 mmol), one equivalent of $AgPF_6$ (20.45 mg, 0.081 mmol), and 5 equivalents of pyridine (0.033 mL, 0.404 mmol) were combined in a round bottom flask. 15.0 mL of acetonitrile was added and the mixture was refluxed overnight. After cooling to room temperature the AgCl was filtered off, and the filtrate was reduced in volume. The residue was dissolved in a minimal amount of dichlomethane and precipitated out with diethyl ether. The resultant orange solid was filtered and washed with diethyl ether. Crystals suitable for X-ray diffraction were grown by vapor diffusion of THF into an acetonitrile solution.

3: Yield: 49 mg (75%). IR (C≡O stretch, cm^{-1}): 1913 (vs), 2031 (s). IR (C═O stretch, cm^{-1}): 1673 (m). ESI MS (positive mode) calcd $C_{28}H_{17}N_3O_5Re$ 662.0727 *m/z*, found 662.0715. ^{1}H NMR (500 MHz, d_6 - DMSO): δ = 9.59 (s, 1H, H–C═N), 9.36 (d, ^{3}J = 4.9 Hz, 1H, H on py), 8.52–8.44 (m, 4H, H on anthraquinone), 8.33 (m, 1H, H on py), 8.28

(m, 4H, H on py and anthraquinone), 8.10 (m, 1H, H on anthraquinone), 8.06 (m, 1H, H on py), 8.00 (m, 2H, H on py and anthraquinone), 7.51 (m, 2H, H on py). ^{13}C NMR (125 MHz, d_6 – DMSO): δ = 189.9 (C═O), 181.8 (C≡O), 181.7 (C≡O), 181.6 (C≡O), 175.3, 155.0, 154.6, 153.9, 153.6, 152.6, 141.9, 140.6, 134.9, 134.8, 134.6, 133.3, 133.2, 133.1, 132.1, 131.8, 129.4, 128.8, 127.3, 127.1, 120.9.

3. Results and discussion

We were able to synthesize the desired anthraquinone conjugates via the reaction shown in Scheme 1. The reaction of one equivalent of $Re(CO)_5X$ (X = Br, Cl) along with single equivalents of both pyridine-2-carboxyaldehyde and 2-aminoanthraquinone in refluxing ethanol produced compounds **1** and **2** in reasonably good yield (1: 64%; 2: 67%). The resultant compounds could be isolated via collection of the precipitate by filtration and washing of the product with hot ethanol. We could also isolate the cationic species **3** upon removal of the halide via use of $AgPF_6$. The reaction of either **1** or **2** in CH_3CN/pyridine with $AgPF_6$ produced the desired compound as a precipitate.

Compounds **1**–**3** were isolated as pure materials by recrystallization, affording single crystals suitable for X-ray structure elucidation. DMSO diffused with H_2O produced single crystals of **1** and **2**, and compound **3** was isolated as a crystalline solid from THF/CH_3CN. We were able to elucidate the structures of all three and the structures of the three compounds are shown in Fig. 1. Selected bond lengths and angles can be found in Table 1. As in other pyca conjugates, the pyridine-2-aldimine unit binds to the metal center as a bidentate chelate, with a facial set of three carbonyls and either the halide or the pyridine occupying the sixth position on the metal center. The Re–C bonds and the C–O bonds in the facial arrangement of carbonyls exhibit typical lengths for these compounds and are in good agreement with our prior work. Similarly, the pyridine-2-aldimine unit possesses similar geometric parameters to other $Re(CO)_3$ pyca complexes. The anthraquinone unit is pendant to the bound imine, and in all complexes is not co-planar with the diimine chelate ring, with angles of ~42, 43, and 51° between the planes of the two sets of rings. The anthraquinone units are all in the fully oxidized state, with C–O bond lengths averaging ~1.22 Å, indicative of double bonds rather than hydroxides.

Spectroscopy was also used to confirm the identity and properties of compounds **1**–**3**. The three compounds exhibit a_1 and e carbonyl infrared bands that correspond to the localized C_{3v} geometry at the metal centrer however the lack of symmetry due to the pyca conjugate ligand splits the e band. The ^{1}H NMR spectrum resonances can be readily assigned (supplementary information), and all three spectra show diagnostic imine C–H signals at ~9.5–9.6 ppm. The UV–visible spectra of compounds **1**–**3** are shown in Fig. 2. The presence of a diimine bound to the metal center results in MLCT bands in the high-energy region of the visible spectrum, which undergo diagnostic solvatochromic shifts depending on the polarity of the solvent, which are approximately 30–40 nm (supplementary information). The extinction coefficients are on the 10^3 range, and not surprisingly are very similar for **1** and **2**. However, for compound **3**, there is a hypsochromic shift in absorption from ~410 nm in DMF to ~390 nm.

We also probed the electrochemistry of compounds **1**–**3** to determine how the conjugation to the $Re(CO)_3$ diimine unit affects the reduction potential of the anthraquinone unit. The cyclic voltammograms of **1**–**3** along with the starting aminoquinone are shown in Fig. 3. The reduction potential of the aminoquinone unit occurs at approximately ~ -1.5 V versus Fc/Fc+ in DMF and the process is quasi reversible. In complexes **1** and **2**, there are multiple non-reversible reductions with the reduction for the aminoquinone unit taking place at much more positive potentials (~1.1 V versus Fc/Fc+). For compound 3, where the positive charge on the complex results in a further positive shifting of the redox potential of the anthraquinone unit to ~ -0.94 V versus Fc/Fc"; since the bonding is nearly identical as that in 1 and 2, we can ascribe this shift entirely due to electrostatic effects.

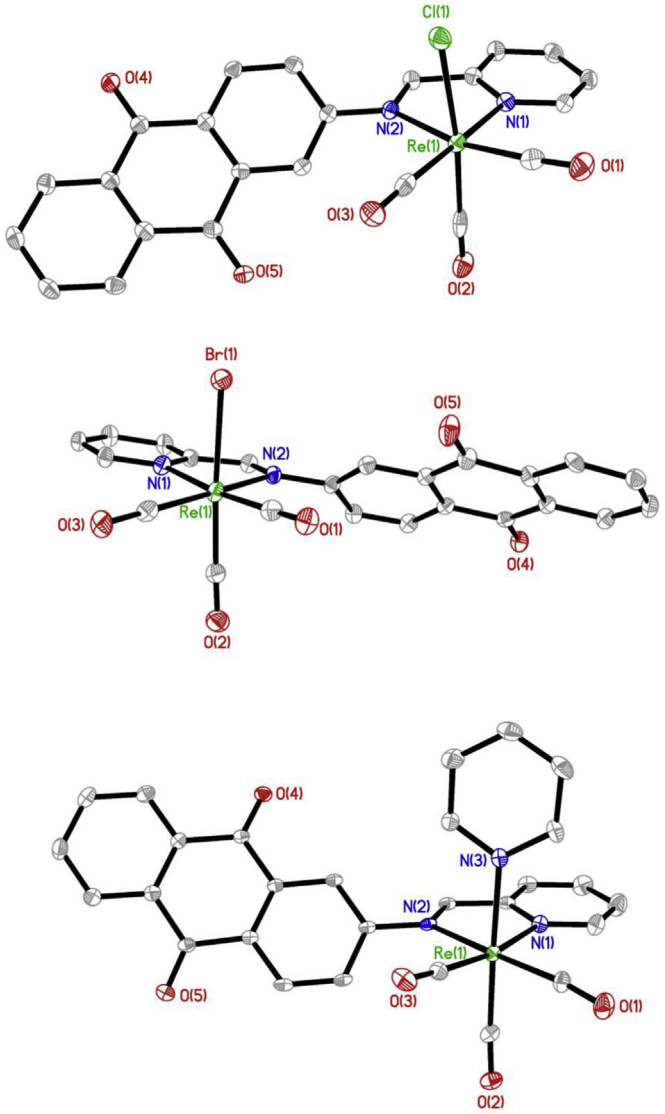

Fig. 1. The structures of compounds **1**–**3** (top to bottom) with 35% thermal ellipsoids. Hydrogen atoms have been omitted for clarity.

Table 1
Selected bond lengths and angles for compounds **1**–**3**.

	1	2	3
Re–$C_{(Carbonyl)}$	1.923(5)	1.926(7)	1.919(6)
	1.98(2)	1.945(13)	1.924(6)
	1.929(5)	1.922(6)	1.923(6)
Re-N_{imine}	2.174(4)	2.179(5)	2.169(5)
Re-$N_{pyridine}$	2.192(4)	2.192(5)	2.179(5)
C–$O_{(C=O)}$	1.141(6)	1.151(8)	1.152(7)
	1.07(2)	1.166(14)	1.147(7)
	1.146(6)	1.145(8)	1.151(7)
anthraquinone	1.224(5)	1.224(7)	1.226(7)
C–$O_{(C=O)}$	1.214(5)	1.217(8)	1.218(7)
Re–$X_{(Cl, Br, N(pyr))}$	2.413(5)	2.5681(14)	2.192(7)
N1–Re–N2	74.15(13)	74.36(18)	74.68(18)

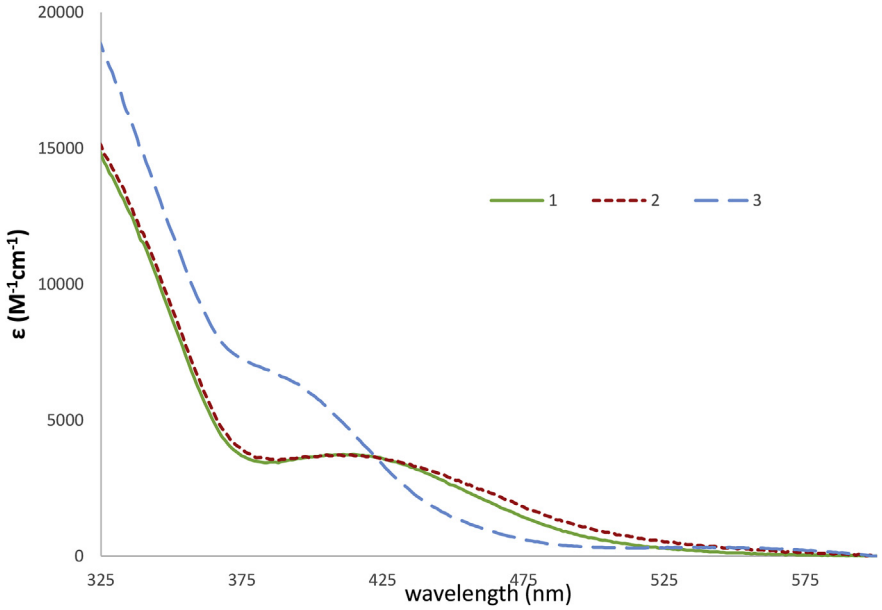

Fig. 2. UV–visible spectra for compounds **1**–**3** in DMF.

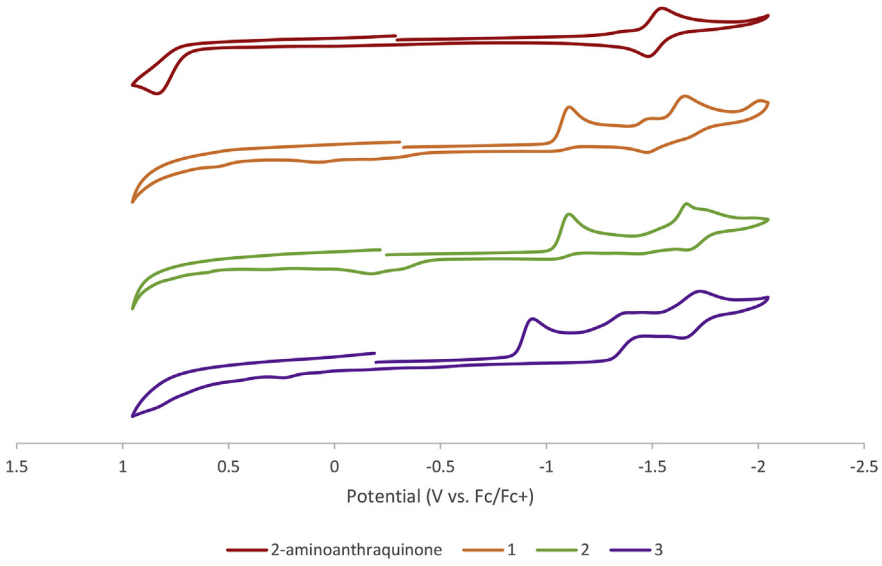

Fig. 3. Cyclic voltammograms for 2-aminoquinone and compounds 1-3 in DMF. All potentials were measured versus Fc/Fc^{+} at a scan rate of 50 mV/s.

4. Conclusions

In conclusion, we were able to readily synthesize a series of anthraquinone conjugates with $Re(CO)_3$ using the pyca strategy. This method allows for one-pot conditions, resulting in a diimine with a pendant anthraquinone directly attached to the chelating unit. The halides can be removed and replaced with a pyridine to afford a cationic complex. As in other $Re(CO)_3$ diimines, compounds **1**–**3** exhibit MLCT bands, with the pyridine adduct hypsochromically shifted relative to those of the chloride and bromide. We also investigated their electrochemical behaviour, and the pyridine complex undergoes reduction at a more positive potential than the chloride or bromide, and all are more positive than aminoquinone alone. We are continuing our investigations into compounds **1**–**3** including their interactions with DNA and biological activity.

Declarations of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jorganchem.2018.10.023.

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