Effects of Substituted Triarylphosphine Ligands on Electron Transfer in [(*p*-cymene)Ru] Complexes

Anthony N. Micci,[a] Julia E. Fumo,[a] Robert D. Pike,[b] Davide Lionetti[a,*]

[a] Department of Chemistry, Franklin & Marshall College, P.O. Box 3003, Lancaster, PA 17604, USA

[b] Department of Chemistry, College of William & Mary, P.O. Box 8795, Williamsburg, VA 23187, USA

* corresponding author: dlionett@fandm.edu

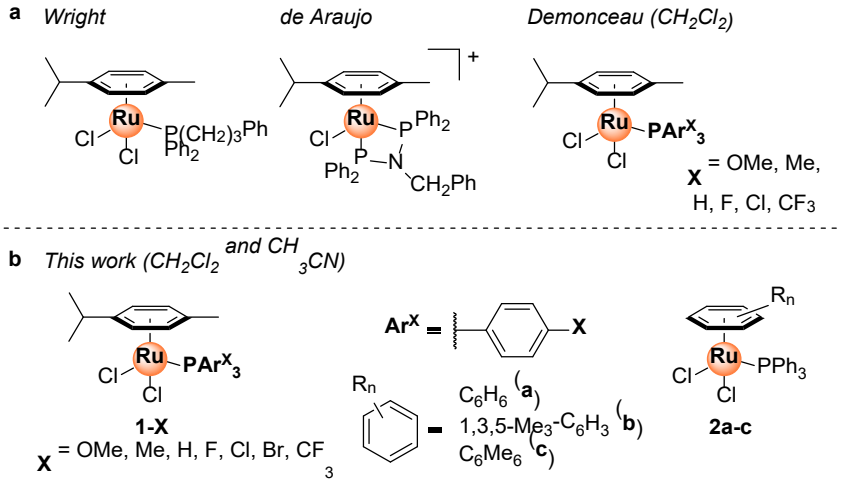
Abstract: The consequences of electron transfer in ruthenium-arene catalysts supported by triarylphosphine ligands has not been fully elucidated in coordinating solvents, which are known to engender further transformations in analogous Ru species upon oxidation and may reveal new modes of reactivity in these compounds. Herein, we report electrochemical studies of (*p*-cymene)$RuCl_2(PAr^X_3)$ complexes containing substituted triarylphosphines (PAr^X_3) and the effects of the ligand substituents on ET processes. These complexes undergo ET at potentials that depend on the ligand substituents (X); in CH_3CN, electrochemical oxidation generates new products whose formation and ET behavior also depend on these substituents. Based on evidence for loss of cymene in these transformations, the products of these reactions are formulated as the tris(nitrile) complexes $(PAr^X_3)RuCl_2(NCCH_3)_3$.

Half-sandwich complexes of ruthenium(II) of the form (*p*-cymene)$RuCl_2(PR_3)$ (PR_3 = phosphine or phosphite ligand) have attracted significant interest due to their relevance to the fields of coordination chemistry,[1-3] catalysis,[4] and biochemistry.[5-7] Complexes of this type and their derivatives are known to be versatile catalysts, facilitating numerous organic transformations such as hydrogenation of olefins,[8-9] carbonyl compounds,[10-13] and CO_2,[14] hydration of nitriles,[15-16] addition of carboxylic acids to alkynes,[17-19] ring-opening metathesis polymerization (ROMP),[20-21] and atom-transfer radical addition[21-22] and polymerization[23-24] (ATRA/ATRP) reactions. Compounds in this family also possess cytotoxic properties;[25-26] their potential use as anticancer agents has thus been the focus of a growing number of intriguing reports.[27-30]

Conversely, the electron transfer (ET) properties of (*p*-cymene)$RuCl_2(PR_3)$ complexes have received less attention than they deserve given the insight they could provide into strategies to tune activity in various contexts. The few investigations in this context have revealed that these complexes undergo $1e^-$ oxidation to Ru(III) at potentials that depend on the phosphine ligand platform and the Ru coordination environment.[15,31-35] Furthermore, the fate of the nascent Ru(III) species appears dependent on experimental conditions; in coordinating solvents, electrochemically irreversible oxidations lead to formation of new

electroactive products.[28,30,36-37] In reports by Wright[36] and de Araujo,[28] involving diphenyl(3-phenylpropyl)phosphine or chelating bis(phosphine) platforms (Chart 1a), respectively, such products have been identified as tris(nitrile) complexes resulting from the dissociation of *p*-cymene and binding of CH_3CN upon oxidation to Ru(III).

Chart 1. [(*p*-cymene)Ru] complexes supported by PR_3 ligands.



Analogous studies of complexes supported by triarylphosphine ligands, the most widely studied subset of compounds in this family, would be of particular interest. Demonceau and coworkers reported cyclic voltammetry (CV) data for a series of (*p*-cymene)$RuCl_2(PAr^X_3)$ complexes (Ar^X = 4-X-C_6H_4, X = OMe, Me, H, F, Cl, CF_3); Chart 1a), revealing a significant influence of the X substituents on the Ru(III/II) reduction potential,[22] which was correlated with their catalytic competence in the Kharasch addition–an ATRA reaction involving ET during catalysis. However, as these studies were carried out in non-coordinating dichloromethane (CH_2Cl_2) solvent, no ET-induced reactions were observed.[28-30] Investigations involving coordinating solvents would reveal how such reactivity is modulated by the substituted phosphine ligands, providing insight that could be valuable in further assessing catalytic competence. To assess how coordinating solvents affect ET in these systems, we report chemical and electrochemical studies of an expanded series of (*p*-cymene)$RuCl_2(PAr^X_3)$ complexes (**1-X** = OMe, Me, H, F, Cl, Br, CF_3; Chart 1b) in coordinating solvent, including chemical reactivity of the nascent Ru(III) species. The influence of the substituents on ET in these complexes and the reactivity of their Ru(III) compounds are discussed.

Complexes **1-X** are prepared in good yields from the well-known [(*p*-cymene)$RuCl_2$]$_2$ precursor.[38] Hitherto unreported **1-Br** was characterized via nuclear magnetic resonance (NMR) spectroscopy and single-crystal X-ray diffraction (XRD). The solid-state structure of **1-Br** (Figure S40) reveals the expected *pseudo*-octahedral environment at Ru, with an η^6-cymene motif, two chlorides, and the Br-substituted

triarylphosphine ligand. The bond and angle metrics (Table S2) are in agreement with those of other compounds in this series, indicating minimal effects of the phosphine substituents on the structural properties of these compounds.

While stable in the solid state for several years, compounds **1-X** undergo substantial speciation in solution; although ligand exchange processes have been studied in the context of various applications,[26,39-40] speciation of these complexes in organic solvents has not been fully elucidated.[41-43] The slow, light-dependent decomposition of **1-X** compounds in chlorinated solvents (Figures S11-S16) is consistent with their reactivity towards CCl_4 in ATRA catalysis.[21-22] In CH_3CN, compounds **1-X** decompose more rapidly (Figure S17-S22) generating multiple products, including species consistent with exchange of Cl^- with CH_3CN to give solvento species.[30,44] In both solvents, free *p*-cymene was generated unless light was excluded, indicating dissociation of the arene fragment in these solutions; in the absence of light, however, no *p*-cymene was detected, suggesting that a photolysis pathway may be operative in ligand exchange.

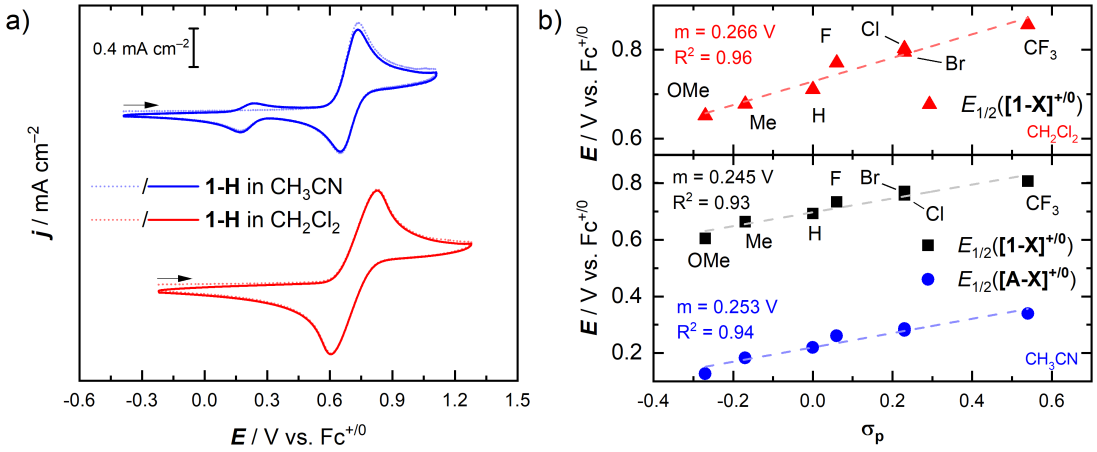


Figure 1. a) CV data for **1-H** in CH_2Cl_2 (0.1 *M* [^{n}Bu$_4$N][PF$_6$], 100 mV/s; lower trace) and CH_3CN (0.1 *M* [^{n}Bu$_4$N][PF$_6$], 100 mV/s; upper trace). Dotted/solid lines correspond to the first/second CV cycles, respectively. b) Plots of $E_{1/2}$(**[1-X]**$^{+/0}$) in CH_2Cl_2 vs. σ_p (upper panel) and of $E_{1/2}$ (**[1-X]**$^{+/0}$) and $E_{1/2}$(**[A-X]**$^{+/0}$) in CH_3CN vs. σ_p (lower panel). The slopes (m) for the lines of best fit are included.

In agreement with the report by Demonceau,[22] CV data collected for complexes **1-X** in CH_2Cl_2 reveal a virtually reversible 1e$^-$ event at potentials between +0.6 and +0.8 V vs. the ferrocenium/ferrocene couple (denoted hereafter as Fc$^{+/0}$; Figure 1a), consistent with oxidation from Ru(II) to Ru(III). The X substituents significantly affect the reduction potential for this couple, with a ~180 mV shift observed across this series, with electron-withdrawing substituents resulting in more positive reduction potentials and vice versa (Table 1). To quantify substituent effects, we employed the well-known *para* Hammett parameters (σ_p),[45] which have been extensively used to generate free energy relationships in organic electrochemistry[46-48] and have

been implemented in inorganic systems involving both metal- and ligand-centered ET events.[49-55] A plot of the midpoint potentials ($E_{1/2}$) for the **[1-X]$^{+/0}$** couple vs. σ_p reveals a linear correlation (Figure 1b, upper panel), establishing the applicability of σ_p values in quantifying the electronic properties of the X substituents in this system. Though a Hammett analysis was not described in the publication by Demonceau, a similar correlation is observed in the original electrochemical data (Figure S23).[22]

CV analysis in acetonitrile revealed different ET profiles (Figures 1a and 2; Table 1). While the first voltammetric cycle indicated an analogous 1e$^-$ oxidation to Ru(III) as in CH_2Cl_2, the cathodic peak current (i_{pc}) is attenuated vs. its anodic counterpart (i_{pa}; $i_{pc}/i_{pa} \approx 0.75$), indicating substantial irreversibility. Further scanning revealed a new *quasi*-reversible event at a potential ~500 mV more negative than for the initial **[1-X]$^{+/0}$** couple. These observations are consistent with partial conversion of the nascent Ru(III) complexes to new electroactive products, **A-X**. CV data collected at faster scan rates (1,000-2,000 mV/s, Figure S25) indicates that formation of **A-X** can be outcompeted on the CV timescale in this series of compounds.

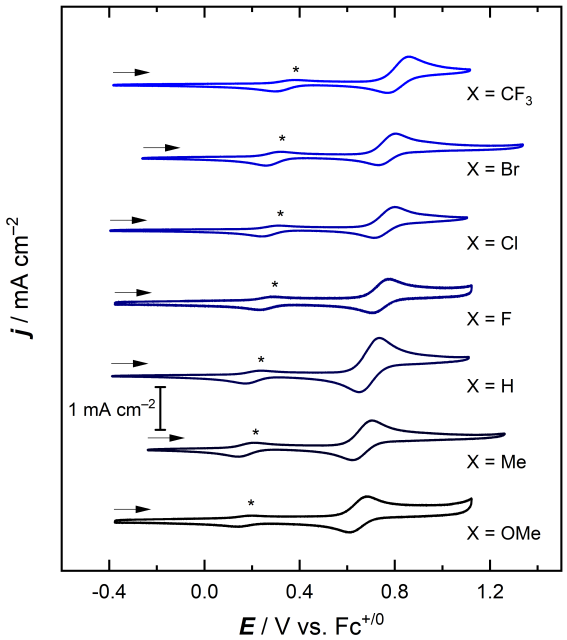


Figure 2. CV data (0.1 *M* [^{n}Bu$_4$N][PF$_6$] in CH_3CN, 100 mV/s) for complexes **1-X**. Only the second voltammetric scans are shown for clarity; events corresponding to **A-X** species are marked with (*).

Addition of CH_3CN to complexes **1-X** in CH_2Cl_2 engenders similar electrochemical behavior to that observed in pure CH_3CN (Figures S26-S32). As generation of **A-X** products is incomplete on the voltammetric timescale in neat CH_3CN ([CH_3CN] ≈ 19.6 *M*, ~6,500 equiv. vs. Ru), large amounts of CH_3CN (500-1,500 equiv.) are necessary to enable clear identification of **[A-X]$^{+/0}$** couples in CH_2Cl_2.[36] Comparison of the effects of CH_3CN addition across the series of **1-X** complexes reveals that the extent of conversion

of the nascent **[1-X]**$^+$ species to the corresponding **[A-X]**$^+$ complexes is influenced by the phosphine ligand substituents. The ratio between the cathodic peak currents for the reduction of **[1-X]**$^+$ and **[A-X]**$^+$, a proxy for the extent of this reaction, displays an intriguing correlation with σ_p, with more electron-withdrawing substituents displaying greater conversion to **A-X** byproducts (Figure S34). This observation supports an associative mechanism for the reaction of **[1-X]**$^+$ complexes with CH_3CN (*vide infra*), consistent with the well-precedented associative ligand exchange in analogous 17e$^-$ complexes.[56-59]

Table 1. Reduction potentials[a] for complexes 1-X, A-X, and 2a-c

Complex	σ_p (X)[b]	$E_{1/2}$ (**[1-X]**$^{+/0}$) CH_2Cl_2	$E_{1/2}$ (**[1-X]**$^{+/0}$) CH_3CN	$E_{1/2}$ (**[A-X]**$^{+/0}$) CH_3CN
1-OMe	–0.27	0.63	0.65	0.17
1-Me	–0.17	0.65	0.66	0.18
1-H	0	0.71	0.70	0.21
1-F	0.06	0.73	0.74	0.25
1-Cl	0.23	0.76	0.76	0.27
1-Br	0.23	0.76	0.77	0.29
1-CF$_3$	0.54	0.81	0.81	0.34
2a	-	-	0.91[c]	0.21
2b	-	-	0.66	[d]
2c	-	-	0.53	[d]

[a] in V vs. $Fc^{+/0}$; [b] from reference [45]; [c] E_{pa}; [d] only minimal byproduct observed

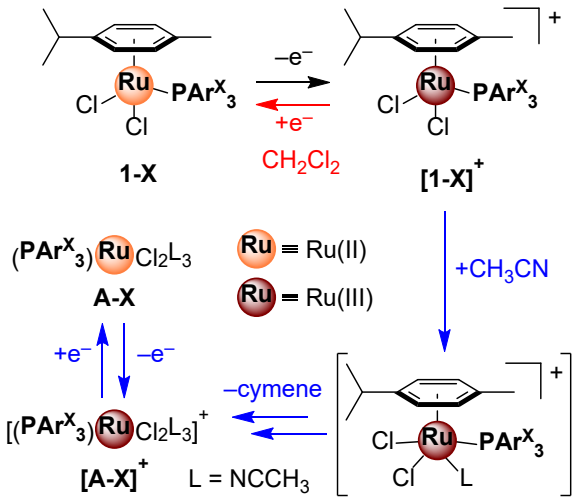
A plot of $E_{1/2}$(**[1-X]**$^{+/0}$) values in CH_3CN vs. σ_p reveals a linear correlation (Figure 1b). Notably, the potentials for the **A-X** products ($E_{1/2}$(**[A-X]**$^{+/0}$)) also correlate linearly with the σ_p parameters (Figure 1b), suggesting retention of the PAr^X_3 ligands in these complexes. Furthermore, the similarity between these correlations suggests that the number of phosphine ligands is unchanged in complexes **A-X**, as formation of bis(phosphine) compounds would result in a stronger dependence on σ_p due to the increased number of substituents, while no dependence on σ_p would be expected for phosphine-free species.

To compare the effects of substituents X on reduction potential in this series to those observed in literature systems, the Hammett reaction constant, ρ, was determined using equation (1):

$$\Delta E = 0.0592\rho(\Sigma\sigma_p) \quad (1)$$

By plotting the *shift* in potential (ΔE) for complexes **1-X** with respect to unsubstituted analogue **1-H** vs. the sum of Hammett parameters for all substituents ($\Sigma\sigma_p$), a linear correlation should be obtained whose slope can be used to calculate ρ (Figure S36).[46-47] Analysis of complexes **1-X** and **A-X** yields ρ values of 1.21 and 1.27, respectively, in line with known values for systems in which substituents are located at a comparable distance (5-7 bonds) from the redox-active metal center (ρ = 0.8–1.5).[54,60-64] Furthermore, the similar ρ values obtained for the two series of compounds corroborate the assignment of **A-X** compounds as mono-phosphine complexes. Hammett analysis data based on incorrect $\Sigma\sigma_p$ values (e.g. $6\sigma_p$ for **A-X**) would yield significantly different values of ρ for **A-X** vs **1-X**; this would be inconsistent with the expected similar electronic communication between X and with Ru in both **1-X** and **A-X** compounds, which should be reflected in similar values of ρ for both series.

Scheme 1. Proposed reactivity of 1-X complexes.



Based on the precedent for substitution of cymene by CH_3CN upon oxidation to Ru(III),[28,36] we tentatively assign products **A-X** as the corresponding acetonitrile complexes $(PAr^X{}_3)RuCl_2(NCCH_3)_3$ (Scheme 1). Attempted synthesis of **A-H** via chemical oxidation, thermolysis,[28] or bulk electrolysis,[36] however, yielded mixtures of phosphine-containing products, with minimal amounts of **A-H** detected via CV. Still, observation of free *p*-cymene in these mixtures was consistent with its postulated dissociation upon oxidation. To provide additional evidence for ligand exchange, literature analogues of **1-H** supported by other arene ligands (**2a-c**, Chart 1b) were investigated via CV; in the course of these studies, the solid-state structure of **2b**, hitherto unreported in the literature, was also obtained (Figure S41, Table S3).[15,65-67] As these compounds contain the same triphenylphosphine ligand, arene dissociation should generate the same byproduct, **A-H**. Complex **2a**, supported by a benzene ligand, undergoes an irreversible oxidation at E_{pa} = +0.84 V vs. $Fc^{+/0}$ in CH_3CN (Figure S38); this potential is ~100 mV more positive than for the oxidation of

1-H, consistent with the absence of electron-donating substituents on the arene ligand in **2a**. A new product is also observed in the CV data whose reduction potential ($E_{1/2}$ = 0.21 V) is identical to that for the new species (**A-H**) that is generated electrochemically from **1-H**. The formation of the same byproduct from **2a** and **1-H** despite their different arene ligands is consistent with arene dissociation during the chemical reaction that follows oxidation to Ru(III) and further supports the assignment of compounds **A-X**.

Surprisingly, complexes **2b** and **2c**, containing mesitylene and hexamethylbenzene ligands, respectively, undergo virtually reversible oxidation events with minimal generation of new byproducts (Figure S38). **2b** and **2c** are oxidized at less positive potentials than **1-H** (Table 1), consistent with the greater number of electron-donating substituents in these complexes. Hammett analysis of the potentials for complexes **1-H** and **2a-c** as a function of arene ligand substituents (Figure S39) yields a value of ρ that is significantly larger (4.54) than for the effects of the phosphine ligand substituents in **A-X** complexes (1.21), suggesting that electronic communication between ligand substituents and Ru is substantially stronger when these functionalities are placed on the arene ligand. The irreversibility of the oxidation of **2a** and the generation of minimal **A-H** upon oxidation of **2b-c** further corroborate the associative mechanism of ligand exchange: sterically bulkier arene ligands disfavor binding of CH_3CN to Ru(III), resulting in virtually reversible electrochemical events. Conversely, the unsubstituted benzene in **2a** facilitates CH_3CN binding and faster conversion to **A-H**, leading to the observed electrochemical irreversibility. Electrochemical studies to further characterize complexes **A-X** and provide additional confirmation of their identity are currently ongoing.

In conclusion, electrochemical characterization of (*p*-cymene)$RuCl_2(PAr^X_3)$ complexes in coordinating solvent revealed that $1e^-$ oxidation to Ru(III) initiates a chemical transformation that generates new electroactive products, **A-X**, with reduction potentials ~500 mV more negative than that of the original compounds. Based on precedent for exchange of cymene with CH_3CN and on data supporting retention of the phosphine ligand and loss of cymene during (electro)chemical oxidations, these products can be assigned as complexes $(PAr^X_3)RuCl_2(NCCH_3)_3$; while stable on the electrochemical timescale, these products could not be generated chemically. In conjunction with the solution instability of **1-X** complexes, these results highlight the role of solvent in ET-coupled reactivity in these systems and in promoting speciation of these complexes in solution. The effects of ligand functionalization on these processes further provide possible methods for tuning activity under catalytic or biochemical conditions.[68]

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Author Contributions

Project design, D.L.; synthesis, characterization, and data collection, A.N.M., J.E.F., and D.L.; X-ray data collection and analysis, R.D.P.; writing–original draft, D.L.; writing–review and editing, A.N.M., J.E.F., R.D.P., D.L. All authors have given approval to the final version of the manuscript.

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