

Electrochemical Oxidation and Nucleophilic Addition Reactions of Metallocenes in Electrospray Mass Spectrometry

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Metallocenes, substituted metallocenes, and organometallic salts containing metal–carbon bonds have been investigated by electrospray mass spectrometry (ESMS). Organometallic salts yielded stable cations in high abundances; metallocenes appeared in the oxidized form [i.e., as bis(cyclopentadienyl) metal cations, Cp_2M^+]. Identifications were confirmed by inspection of the natural isotope distribution patterns. ESMS response vs concentration (log–log) plots showed a linear range between 10^{-9} and 10^{-5} M for both Cp_2Fe and $[\text{Cp}_2\text{Fe}]^+[\text{PF}_6]^-$. For solutions of equivalent concentration, however, the salt form always yielded a higher abundance of Cp_2Fe^+ . Neutral metallocenes are ionized by an electrochemical oxidation (electron-removal) mechanism at or near the electrospray (ES) capillary (needle). Increasing electrospray appearance potentials for Cp_2M^+ (M = metal) formation correlated with increasing half-wave potentials for oxidation [$E_{1/2}(\text{ox})$] and increasing ionization energies (IE) in the series: decamethylferrocene, 1,1'-dimethylferrocene, ferrocene, formylferrocene, carboxylferrocene, acetylferrocene, 1,1'-diacetylferrocene, osmocene, and ruthenocene. For osmocene [relatively high $E_{1/2}(\text{ox})$ and IE], ESMS conditions were established whereby protonation was competitive with oxidation, thus creating two pathways of ion formation. In methylene chloride solvent, chloride ion was incorporated into the inner sphere of certain metallocenes subjected to ESMS, forming Cp_2RuCl^+ and Cp_2OsCl^+ complexes via nucleophilic addition. These latter Ru(IV) and Os(IV) species also formed analogous gas-phase complexes with trifluoroacetate ion and hydroxide ion. Results have been rationalized on the basis of ion stability considerations.

The development of organometallic chemistry was greatly stimulated by the discovery of bis(cyclopentadienyl) iron, i.e., “ferrocene” ($\eta^5\text{-C}_5\text{H}_5$)₂Fe in 1951.¹ Since then, the cyclopentadienyl ligand (Cp) has continued to play a key role in the evolution of this field. As of the early 1990s, more than 80% of all synthesized organometallic complexes of transition metals contained the cyclopentadienyl ligand or its derivatives.² Metallocenes [i.e., bis(cyclopentadienyl) metal complexes, abbreviated Cp_2M] are important precursors for the synthesis of a wide variety of organometallic compounds. Furthermore, water-soluble $[\text{Cp}_2\text{Fe}]^+$ (ferricinium) salts and $[\eta^6\text{-(arene)}_2\text{Fe}]^{2+}$ salts have been found to have significant antitumor

activity.³ Köpf-Maier et al.⁴ reported benzene-substituted metallocenes of group 14 elements (i.e., $[(\text{C}_6\text{H}_5)_5\text{-C}_5]_2\text{Sn}$ and $[(\text{C}_6\text{H}_5)_5\text{C}_5]_2\text{Ge}$) as new types of nonplatinum antitumor agents.

Among all the organometallic compounds, metallocenes are perhaps the most highly characterized. Ferrocene has been used extensively as a model redox system for nonaqueous investigations. However, much less information is available for other group 8 metallocene complexes.⁵ Metallocenes usually have lower ionization energies than other organometallic compounds such as carbonyl complexes of the same metal.⁶ In common solvent/electrolyte systems, the oxidation of Cp_2Ru has been reported to occur via an irreversible two-electron process.^{7–12} Under similar conditions, Cp_2Os undergoes an irreversible one-electron oxidation.^{7–12} Taube and co-workers¹³ isolated “osmocinium” as a highly reactive $[\text{Cp}_2\text{Os}]_2^{2+}$ dimer formed by the oxidation of Cp_2Os with Ce(IV) in CH_3CN . This strongly suggests that the irreversible electrochemical oxidation of osmocene is directly linked to the generation and subsequent reaction of the dimeric complex.

Since 1955, a large number of metallocenes and their derivatives have been studied by mass spectrometry.^{14–21} Mass spectrometric investigations of bis(pentamethylcyclopenta-

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dienyl) metal complexes have also been reported.²²⁻²⁴ The ionization techniques used in the earlier studies were electron ionization (EI),¹⁵⁻²³ photoionization,²⁴ and chemical ionization (CI).^{17,23} Generally, EI mass spectra of unsubstituted metallocenes are readily interpretable, showing Cp_2M^+ (M = metal), CpM^+ , M^+ , and low abundances of other fragment ions, while the spectra of substituted metallocene derivatives can be more complicated. Ionization energies (IE) for Cp_2M along with appearance potentials (AP) for fragment ions of Cp_2M^+ have been measured, and some Cp-M bond energies have also been derived.^{18,24} Moreover, the influence of substituent groups (e.g., $\cdot\text{Cl}$, $\cdot\text{Br}$, $\cdot\text{CH}_3$) on AP, IE, and bond energies has been investigated. More recently, fast atom bombardment (FAB)²³ and "surface ionization" (SI)²⁵ have been used in mass spectrometric investigations of metallocenes. To our knowledge, however, other than some preliminary work in our laboratory,²⁶ the use of electrospray ionization mass spectrometry (ESMS) for the study of metallocenes and their derivatives has not been previously reported.

Electrospray ionization can convert analytes in solution into gas-phase ions with little decomposition. ESMS was first investigated by Dole and co-workers^{27,28} 25 years ago, but it has rapidly developed into an analytical tool only since Fenn and co-workers²⁹⁻³² demonstrated its capabilities in determining the molecular mass of biomolecules and polymers such as polypeptides. For these latter analytes, ES ionization is distinguished by its ability to produce multiply charged ions.^{31,33} Basic sites on neutral molecules can accommodate protons or other cations, while anions may be formed chiefly from the removal of acidic protons. Direct formation of molecular cations (M^{++}) from neutral compounds, however, rarely occurs in ESMS.^{32,34}

Ikonomou et al.³⁵ and Cheng et al.³⁶ have used ESMS to investigate ionic metal complexes in aqueous solutions. Poon et al.³⁷ have applied this technique to the study of platinum anticancer agents, e.g., cisplatin [*cis*-dichlorodiammineplatinum(II)], and Van Berkel et al.³⁴ have generated electrospray mass spectra from porphyrins. These latter two ESMS investigations represent studies of coordination compounds containing metal-nitrogen bonds. Siu et al. have reported

ion spray studies of organoarsenic³⁸ and organotin^{39,40} species containing metalloid- and metal-carbon bonds.

In this paper, three synthesized organometallic salts, $[\text{Cp}^*\text{-Ru-benzene}]^+[\text{CF}_3\text{SO}_3]^-$ (1) and $[\text{Cp}^*\text{-Ru-indole}]^+[\text{CF}_3\text{SO}_3]^-$ (2), $[\text{Cp}_2\text{Fe}]^+[\text{PF}_6]^-$ (3); three metallocenes, Cp_2Fe (6), Cp_2Ru (11), and Cp_2Os (12); and six substituted ferrocenes, Cp^*_2Fe [$\text{Cp}^* = \eta^5\text{-(CH}_3)_5\text{C}_5$] (4), $(\text{CH}_3\text{C}_5\text{H}_4)_2\text{-Fe}$ (5), $\text{CpFeC}_5\text{H}_4\text{CHO}$ (7), $\text{CpFeC}_5\text{H}_4\text{COOH}$ (8), $\text{CpFeC}_5\text{H}_4\text{C(O)CH}_3$ (9), and $(\text{CH}_3\text{C(O)C}_5\text{H}_4)_2\text{Fe}$ (10), were studied by ESMS. This paper explores the potential application of ESMS to the analysis of ionic organometallic compounds and neutral metallocenes, each containing transition metal-carbon bonds. The ionization mechanisms involved in generating organometallic ions from metallocenes using the electrospray mass spectrometer have been examined. The formation of reaction products appearing in ES mass spectra of metallocenes has also been rationalized.

EXPERIMENTAL SECTION

Solution Preparation. The organometallic salts $[\text{Cp}^*\text{-Ru-benzene}]^+[\text{CF}_3\text{SO}_3]^-$ and $[\text{Cp}^*\text{-Ru-indole}]^+[\text{CF}_3\text{SO}_3]^-$ [where $\text{Cp}^* = \eta^5\text{-(CH}_3)_5\text{C}_5$] were synthesized as previously reported.⁴¹ Ferrocene (6) was obtained from Matheson, Coleman & Bell Manufacturing Chemists (Norwood, OH); compounds 4, 9, 11, and 12 were purchased from Strem Chemical Inc. (Newport, MA); 7 and 8 were obtained from Sigma Chemical Co. (St. Louis, MO); and 5 and 10 were purchased from Aldrich Chemical Co. (Milwaukee, WI). $[\text{Fe}(\text{C}_5\text{H}_5)_2]^+[\text{PF}_6]^-$ was prepared from ferricinium tetrachloroferrate as reported in the literature.⁴² All sample solutions were prepared using HPLC-grade solvents: methanol, tetrahydrofuran, acetonitrile, or methylene chloride (J. T. Baker Inc., Phillipsburg, NJ). Tetrahydrofuran was purified prior to use by distillation with sodium under a nitrogen stream. The concentration of all sample solutions was 10^{-3} M. Where noted, HPLC-grade trifluoroacetic acid (TFA) (J. T. Baker Inc.) was added to solutions (0.05–1% by volume) just before infusion. All metallocene and substituted metallocene solutions were prepared just prior to analysis to minimize the possibility of air oxidation.

Electrospray Mass Spectrometry. A quadrupole electrospray mass spectrometer (Vestec 201, Vestec, Houston, TX) was used for all experiments; the electrospray ion source has been described previously.⁴³ Sample solutions were introduced through a stainless steel capillary (needle) (100- μm i.d.) held at 1.4–3.5 kV. The distance between the needle and the counterelectrode (nozzle) was held constant. The exit of the needle was situated at the plane corresponding to the base of the nozzle. The temperature of the electrospray chamber was held at $53 \pm 1^\circ\text{C}$ during data acquisition. The sample solution was delivered by a syringe pump (Harvard Apparatus, South Natick, MA) at 1.6 $\mu\text{L}/\text{min}$ through a fused-silica capillary of 100- μm i.d. Presented mass spectra represent the

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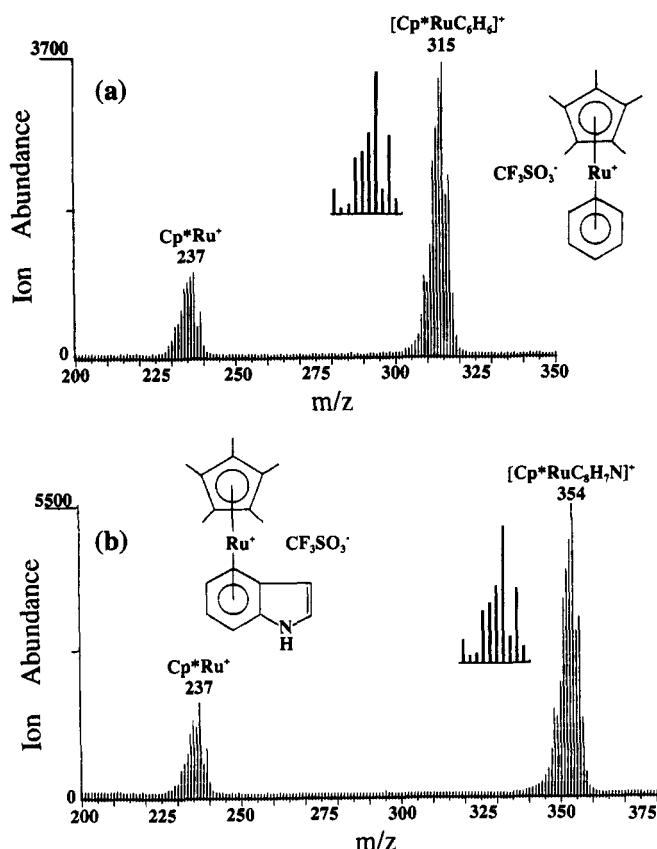


Figure 1. Electrospray mass spectra of organometallic salts in methanol: (a) $[\text{Cp}^*\text{-Ru-benzene}]^+[\text{CF}_3\text{SO}_3]^-$ (10^{-3} M), skimmer-collimator voltage difference (ΔV) = 48 V; (b) $[\text{Cp}^*\text{-Ru-indole}]^+[\text{CF}_3\text{SO}_3]^-$ (10^{-3} M), ΔV = 52 V.

average of at least 10 consecutive scans (approximately 3 s each). The "electrospray appearance potential" for producing intact molecular cations was defined as the minimum electrospray capillary voltage (increasing up from a starting point near 0 V) yielding a peak at the required m/z position with a signal-to-noise ratio of at least 3. Obtained values are quite reproducible when experimental parameters are held constant. During these determinations, the voltage difference between the skimmer and collimator was held at 2 V. In certain other experiments, the skimmer-collimator voltage difference was raised (up to a maximum of +100 V) to promote fragmentations via collision-induced dissociations (CID).

RESULTS AND DISCUSSION

The electrospray mass spectra of two organometallic salts, $[\text{Cp}^*\text{-Ru-benzene}]^+[\text{CF}_3\text{SO}_3]^-$ and $[\text{Cp}^*\text{-Ru-indole}]^+[\text{CF}_3\text{SO}_3]^-$ ($\text{Cp}^* = \eta^5\text{-(CH}_3)_5\text{C}_5\text{H}_5$), in pure methanol obtained under moderate fragmentation conditions are shown in Figure 1. These compounds exhibited very stable ionization and very high sensitivity for the cations $[\text{Cp}^*\text{-Ru-benzene}]^+$ and $[\text{Cp}^*\text{-Ru-indole}]^+$. The isotope distribution patterns for the intact cations were in close agreement with those predicted by natural abundances (shown inset into each spectrum). Relative peak intensities of the lower abundance isotopes may have been raised slightly by incomplete resolution from neighboring peaks. The formed gas-phase cations are likely to be stable solution-phase ions. However, compounds of this type may be difficult to analyze by classical MS ionization techniques (e.g., EI, CI) because of the difficulty involved in vaporizing intact species via heating. When the potential difference

between the skimmer and collimator was elevated to promote CID (Figure 1), $\text{Cp}^*\text{-Ru}^+$ fragment ions were invariably obtained, but no arene- Ru^+ (arene = benzene, indole) ions were observed. Because the loss of the arene radical is much more facile than loss of Cp^* from the 'mixed' complex, the $\text{Cp}^*\text{-Ru}$ bond must be stronger than the Ru-arene bond. This result is in agreement with the findings of Mukerjee et al.⁴⁴ in a study of an analogous molybdenum system.

To evaluate the prospects for generating ion signals representative of metallocenes via the electrospray process, ES mass spectra were obtained for a series of group 8 metallocenes (ferrocene, substituted ferrocenes, ruthenocene, and osmocene), four of which are shown in Figure 2a-d. Significantly, in the molecular ion region, the formation of intact molecular cations via single-electron removal from the neutral species dominates the ES mass spectrum in each case. Proton and cation attachment to neutral metallocenes are minor processes. This is demonstrated by the obtained isotope distribution pattern (e.g., Figure 2d), which closely matches that predicted by natural abundances for Cp_2M^+ species with very minor quantities of protonated molecules present. Moreover, the formation of doubly-charged species was not observed. Under CID conditions, the loss of one of the symmetrically coordinated ligands (leaving as a radical) produced abundant fragments corresponding to CpFe^+ and CpRu^+ (Figure 2, parts b and c, respectively).

Response vs concentration curves for Cp_2Fe^+ (m/z 186) originating from Cp_2Fe and $[\text{Cp}_2\text{Fe}]^+[\text{PF}_6]^-$ are shown in Figure 3. For each compound there is a linear region from 10^{-9} to 10^{-5} M on the log-log plots. At concentrations above 10^{-5} M, the response begins to flatten out. The detection limit for ferrocene is approximately 10^{-9} M, with 0.24 fmol consumed during the generation of the scan data displayed in Figure 3 (signal averaging of 100 0.5-s scans from m/z 150 to 250). Equivalent concentrations of the $[\text{Cp}_2\text{Fe}]^+[\text{PF}_6]^-$ salt gave a higher response than that of ferrocene over the entire concentration range. This indicates that gas-phase ion production via electrochemical oxidation of the neutral compound is less efficient than the transfer of preformed salt ions into the gas phase.

To further examine the processes involved in generating ions from metallocenes and organometallic salts, Table 1 was compiled, listing the solvents utilized and the electrospray appearance potential, i.e., the minimum ES capillary potentials required to generate molecular cations from the respective neutral compounds, as defined in the Experimental Section. In generating the data in Table 1, a skimmer-collimator voltage difference of only 2 V was employed. Under these conditions, CID processes are expected to be negligible, and, indeed, ferrocene (6) and each of the substituted ferrocenes (4, 5, 7-10) produced mass spectra containing ions corresponding to the molecular cations (including isotopes). However, additional ionic species (listed in Table 1) were observed for Cp_2Ru and Cp_2Os . Abundances of the intact molecular cations arising from 10^{-3} M solutions of the respective analytes are ranked in the last column of Table 1. Also listed are ionization energies (IE) and half-wave potentials for electrochemical oxidation $[E_{1/2}(\text{ox})]$.

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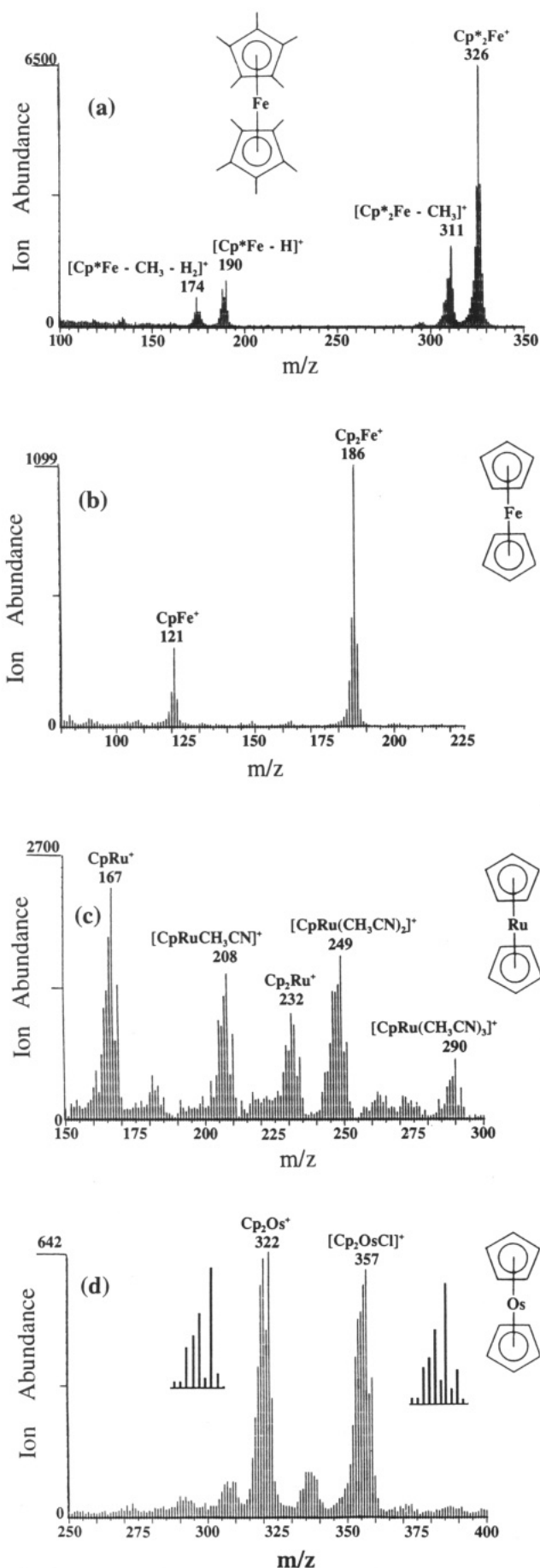


Figure 2. Electro spray mass spectra of metallocenes: (a) decamethylferrocene in CH_3CN (10^{-3} M), skimmer-collimator voltage difference (ΔV) = 55 V; (b) ferrocene in CH_3CN (10^{-3} M), ΔV = 40 V; (c) ruthenocene in CH_3CN (10^{-3} M), ΔV = 17 V; (d) osmocene in CH_2Cl_2 (10^{-3} M), ΔV = 2 V.

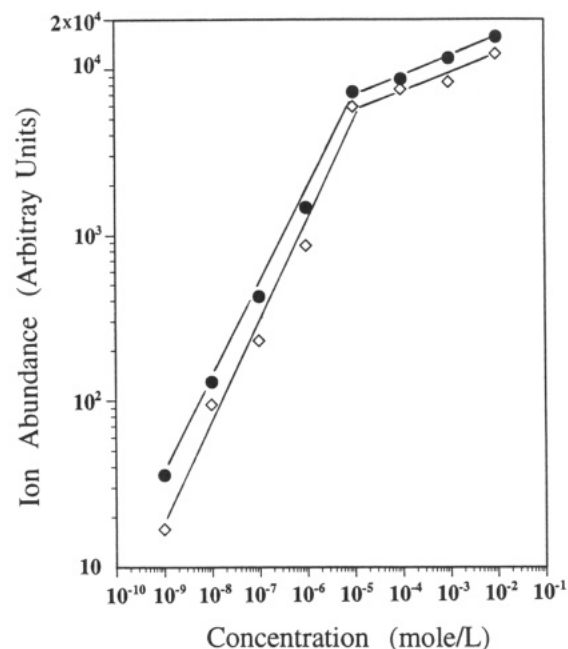


Figure 3. Log-log plot of Cp_2Fe^+ abundance vs concentration for solutions of (●) $[\text{Cp}_2\text{Fe}]^+[\text{PF}_6]^-$ and (◇) Cp_2Fe , each in acetonitrile.

An important result is that higher electrospray appearance potentials correlate to higher $E_{1/2}(\text{ox})$ and ionization energies as shown graphically in Figure 4. For all the organometallic salts (containing preformed ions), the electrospray appearance potentials (~ 1.5 kV, Table 1) are equivalent to the “onset potential for electrospray”. Irrespective of instrument geometry, this onset potential (i.e., the minimum potential required to initiate the electrospray process) has been described to be proportional to the square root of the surface tension of the solution.^{47–49} For the neutral metallocenes, however, the electrospray appearance potential is invariably higher than the onset potential, indicating that below a critical capillary voltage the metallicinium ion cannot be detected even though other ions are being produced by ES. Also noteworthy is that the maximum obtainable signal intensity for identical concentrations of the metallocenes in CH_3CN (10^{-3} M) decreases with increasing IE or $E_{1/2}(\text{ox})$ (Table 1). Cp_2Fe , which has low IE and $E_{1/2}(\text{ox})$ values, exhibited very stable molecular ion production and high sensitivity using relatively low electrospray needle voltages. Excellent ESMS characteristics were also exhibited by Cp^*Fe and $(\text{CH}_3\text{C}_5\text{H}_4)_2\text{Fe}$, which, owing to electron-donating methyl substituents, are each more easily oxidized (lower $E_{1/2}(\text{ox})$ and IE) than ferrocene.^{24,50} The latter complexes exhibited lower electrospray appearance potentials and even higher sensitivities than ferrocene. Cp_2Ru and Cp_2Os , on the other hand, were far more difficult to ionize by ES. For these latter compounds, stable electrospray conditions were difficult to achieve. Optimum conditions yielded comparatively low intensity signals and required the electrospray needle voltage to be undesirably high, i.e., very close to electrical breakdown due to corona discharge.

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Table 1. Summary of Data

no.	compound ^a	MW ^b	IE (eV)	$E_{1/2}(\text{ox})$ (V) ^c	solvent	electrospray appearance potential ^d (kV)	species observed ^e	M ⁺ ion abundance (arbitrary units)
1	[Cp*-Ru-C ₆ H ₅] ⁺ [CF ₃ SO ₃] ⁻	315 ^f			MeOH	1.50 ± 0.05	[M - CF ₃ SO ₃] ⁺	29 376
2	[Cp*-Ru-C ₆ H ₇ N] ⁺ [CF ₃ SO ₃] ⁻	354 ^f			MeOH	1.50 ± 0.03	[M - CF ₃ SO ₃] ⁺	14 836
3	[(C ₅ H ₅) ₂ Fe] ⁺ [PF ₆] ⁻	186 ^f			ACN	1.48 ± 0.02	M ⁺	16 500
4	Cp [*] *Fe	326	5.98 ^h	-0.11 ^g	ACN	1.50 ± 0.02	M ⁺	13 328
5	(CH ₃ C ₆ H ₄) ₂ Fe	214	6.80 ^h	0.245 ^j	ACN	1.85 ± 0.03	M ⁺	3 500
6	(C ₆ H ₅) ₂ Fe	186	7.05 ^h	0.310	ACN	2.10 ± 0.01	M ⁺	3 585
					MeOH/THF	2.20 ± 0.10	M ⁺	5 200
7	C ₅ H ₅ FeC ₆ H ₄ CHO	214	7.30 ^h	0.330	ACN	2.21 ± 0.08	M ⁺	2 290
8	C ₅ H ₅ FeC ₆ H ₄ COOH	230		0.555	ACN	2.46 ± 0.05	M ⁺	1 340
9	CH ₃ C(O)C ₆ H ₄ FeC ₆ H ₅	228	7.20 ^h	0.555	ACN	2.51 ± 0.03	M ⁺ , [M + H] ⁺	1 073
10	(CH ₃ C(O)C ₆ H ₄) ₂ Fe	270	7.40 ^h	0.790	ACN	2.65 ± 0.08	M ⁺ , [M + H] ⁺	881
11	(C ₆ H ₅) ₂ Ru	232	7.81 ⁱ	0.94 ^j	ACN	3.02 ± 0.05	M ⁺ , CpRu(ACN) _n ⁺	790
					CH ₂ Cl ₂ + 0.05% TFA	2.80 ± 0.10	M ⁺ , [M + Cl] ⁺ , [M + TFA - H] ⁺	540
12	(C ₆ H ₅) ₂ Os	322	7.59 ⁱ	0.82 ^j	ACN	2.82 ± 0.10	M ⁺ , [M + OH] ⁺	610
					CH ₂ Cl ₂	2.55 ± 0.10	M ⁺ , [M + Cl] ⁺	642
					CH ₂ Cl ₂ + 0.05% TFA	2.62 ± 0.05	M ⁺ , [M + H] ⁺ , [M + Cl] ⁺ , [M + TFA - H] ⁺	
					CH ₂ Cl ₂ + 1% TFA	1.8 ± 0.05	[M + H] ⁺ , [M + Cl] ⁺ , [M + TFA - H] ⁺	

^a Cp* = (CH₃)₅C₅. ^b Relative molecular mass (Da) corresponds to the most abundant isotope of each metal. ^c Displayed values vs SCE in acetonitrile (Hennig et al.⁴⁵). ^d The "electrospray appearance potential" is defined in the Experimental Section. ^e Species observed under conditions (electrospray capillary potential, skimmer-collimator voltage difference) to achieve the highest sensitivity molecular ions or [M + H]⁺; in each case M refers to the neutral molecule named in the first column. ^f Relative molecular mass (Da) corresponds to that of the cation. ^g From Geiger et al.⁵ ^h From Friedman et al.¹⁵ ⁱ From Müller and D'Or.¹⁶ ^j Displayed values vs SCE. Original measurements were made in acetonitrile using Ag/AgClO₄ reference electrode (Denisovich et al.⁴⁶) which has a potential of +0.343 V with respect to SCE. ^k From Al-Saeed et al.²¹ ^l From Hoh et al.⁸

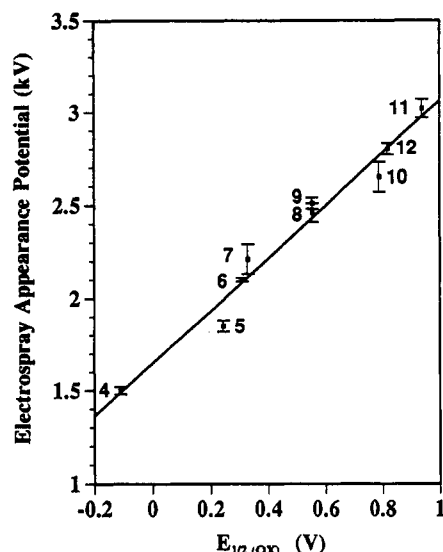


Figure 4. Electro spray appearance potentials of metallocenes (10⁻³ M in acetonitrile) vs $E_{1/2}(\text{ox})$. Compounds are (4) Cp^{*}*Fe, (5) (CH₃C₆H₄)₂Fe, (6) Cp₂Fe, (7) CpFeC₆H₄CHO, (8) CpFeC₆H₄COOH, (9) CpFeC₆H₄C(O)CH₃, (10) (CH₃C(O)C₆H₄)₂Fe, (11) Cp₂Ru, and (12) Cp₂Os. The line was generated by a least-squares linear regression ($r = 0.972$, $n = 9$).

Mechanism of Molecular Ion Formation for Metallocenes.

The precise mechanisms of ion formation in electrospray mass spectrometry are still under debate. Usually ionic species and compounds with acidic or basic sites give the best performance in ESMS. The observation that the electrospray appearance potential for the metallocinium ion increases with increasing $E_{1/2}(\text{ox})$ of the metallocene, while the relative response decreases, provides strong evidence that the molecular ions were produced by an electrochemical oxidation process occurring either in solution or at the needle/solution interface. In other words, the ES source performs functions of an electrolytic cell, as proposed by Blades et al.⁵¹ One may

hypothesize that Cp₂M⁺ could also be produced by chemical oxidation in air. In fact, all the metallocenes used in this study are "air stable", though we noticed that the color of the Cp₂*Fe solution could change from yellow, when freshly prepared, to green after several hours of storage. We presume this color change to be indicative of the oxidation of Cp₂*Fe to Cp₂*Fe⁺ because Cp₂Fe undergoes a similar color change from brownish-yellow to blue-green upon oxidation to Cp₂-Fe⁺.⁵²

Electrospray experiments were repeated using Cp₂Fe in the presence of a strong oxidizing agent, i.e., (10⁻³ M) Cu(II)/CH₃CN [Cu²⁺/Cu(CH₃CN)₂⁺ $E^0 = 0.96$ V vs SCE⁵³]. As compared with results obtained for ferrocene in CH₃CN, the absolute intensity of the Cp₂Fe⁺ peak was observed to approximately double in the presence of Cu²⁺/CH₃CN, indicating that the reagent was successful at producing oxidized Cp₂Fe⁺ in solution. Moreover, the electrospray appearance potential fell from 2.1 kV (in the absence of Cu²⁺) to 1.45 kV (in the presence of Cu²⁺). The latter value is about the same as the electrospray appearance potential observed for ionic organometallic salts (Table 1). This observation provides additional evidence that ESMS production of molecular cations from solutions devoid of the oxidizing agent is occurring via an electrochemical oxidation process. The increase in the intensity of the Cp₂Fe⁺ peak after chemical oxidation in solution underscores the fact that the efficiency of the employed electrospray device as an electrochemical cell is limited, i.e., a significant amount of the neutral compound remained in

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the neutral form in the absence of a solution-phase oxidizing agent.

Solvent Effects. The choice of solvent plays an important role in determining the sensitivity and types of ions formed in the electrospray process. For ferrocene and decamethylferrocene, high sensitivity signals for the molecular cation were achieved using methanol, THF, acetonitrile, or methylene chloride. In contrast, molecular cations of ruthenocene and osmocene were not detected in methanol, in THF, or in a mixture of the two solvents. In acetonitrile and methylene chloride, however, molecular cations Cp_2Ru^+ and Cp_2Os^+ were successfully detected. The solvent influence on the ability to observe Cp_2M^+ and on the ability to form other observed ions can be attributed to stability considerations. Group 8 neutral metallocenes and the cations $[\text{Cp}^*\text{Ru-benzene}]^+$ and $[\text{Cp}^*\text{Ru-indole}]^+$ are all diamagnetic 18-electron compounds. Eighteen-electron organometallics are known to be highly stable in solution as well as in the gas phase. In the presence of appropriate counter-anions such as PF_6^- , BF_4^- , etc., the oxidized product of ferrocene (ferricinium ion) Cp_2Fe^+ (17 valence electrons) is stable in polar solvents such as methanol, acetonitrile, methylenechloride, THF, and water. However, the ferricinium salt will precipitate from nonpolar or less polar solvents such as CCl_4 or diethyl ether.⁵⁴

Van Berkel et al.³⁴ reported the observation of radical cations in electrospray mass spectra of alkyl-substituted metalloporphyrins, polycyclic aromatic hydrocarbons, and other compounds. In their discussion of the effect of solvent systems, they concluded that methylene chloride was one of the best solvents for the detection of radical cations by ESMS, while protic solvents as well as nucleophilic solvents (e.g., water and methanol) should be avoided. Our present results are in general agreement with theirs, but we emphasize that the stability of the specific molecular ion is determinant in dictating whether a given ion will appear in the ES mass spectrum. As long as a certain degree of solvent polarity exists, additional specific solvent properties exerted no obvious effect upon the detectability of molecular ions that are known to possess considerable stability (e.g., Cp_2Fe^+ and Cp^*_2Fe^+). Van Berkel et al.³⁴ also found that adding 0.05–0.1% TFA may stabilize radical cations and enhance M^+ signals. In our present work, we found that the presence of TFA had a negligible effect on the intensity of Cp_2Ru^+ , Cp_2Fe^+ , and Cp^*_2Fe^+ signals. Interestingly, the addition of a small amount of TFA (up to 1%) was ineffective at producing protonated metallocene species $[\text{M} + \text{H}]^+$ for Fe or Ru, but rather effective at producing $[\text{M} + \text{H}]^+$ from osmocene (Figure 5b). $[\text{M} + \text{H}]^+$ was also formed in low abundance from **9** and **10**, which contain acetyl substituents. A competition between protonation and oxidation was thus established, with different optimal conditions existing for each process. Logically, both instrumental considerations (e.g., needle voltage, temperature) and solvent considerations (e.g., proton availability, radical stabilization ability) could influence the relative abundances of protonated vs electrochemically oxidized molecules; doubly-protonated ions were not observed.

It has been proven by $^1\text{H-NMR}$ spectroscopy that, in solution, ferrocene, ruthenocene, and osmocene can be protonated at the metal site using a strong, nonoxidative acid

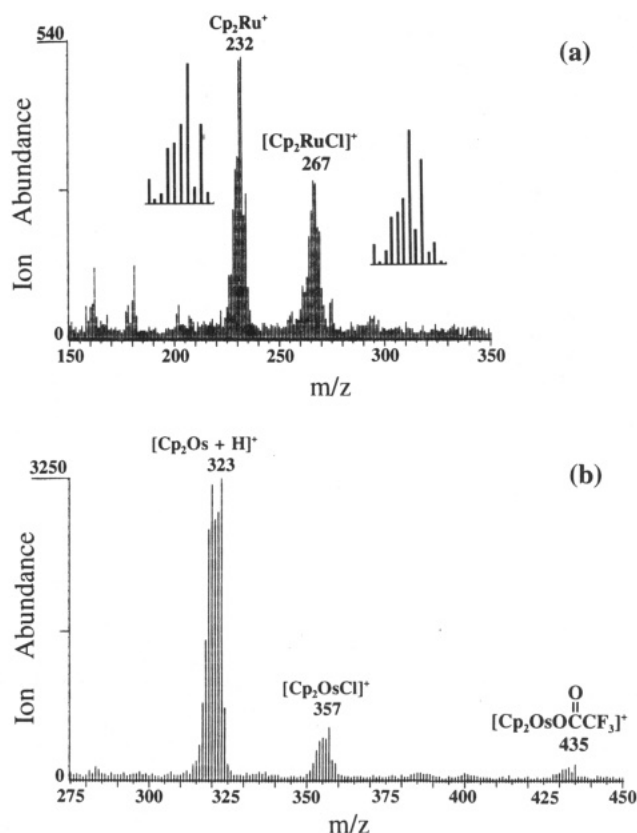
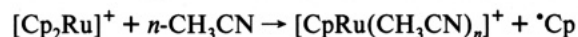


Figure 5. Electrospray mass spectra of (a) ruthenocene (10^{-3} M) in CH_2Cl_2 + 0.05% TFA; (b) osmocene (10^{-3} M) in CH_2Cl_2 + 1% TFA.

(e.g., $\text{BF}_3 \cdot \text{H}_2\text{O}$).⁵⁵ In solution, ferrocene is the most highly protonated metallocene in the series: ferrocene, ruthenocene, and osmocene. Proton affinity data⁶ show that Cp_2Ru is more easily protonated than Cp_2Fe in the gas phase [$\text{PA}(\text{Cp}_2\text{Fe}) = 213$ kcal/mol, $\text{PA}(\text{Cp}_2\text{Ru}) = 220$ kcal/mol]; however, no data were found for Cp_2Os . Our present results indicate that ion formation via protonation is most favorable relative to electrochemical oxidation for osmocene as compared to ferrocene or ruthenocene. This is consistent with the trend of increasing basicity of deprotonated hydrides with downward movement within the same group of metals in the periodic table.^{56,57} For ferrocene, substituted ferrocenes, and ruthenocene, ionization via electrochemical oxidation is heavily favored over protonation in ESMS.

The solvent may also participate in complexation with the metallocene to invoke its decomposition, such as is likely to occur for the ruthenium complex $[\text{Cp}_2\text{Ru}]^+$ in acetonitrile:



The reaction may occur in a stepwise fashion, and the maximum value for n is 3. Therefore, the peaks corresponding to $[\text{CpRu}(\text{CH}_3\text{CN})_n]^+$ shown in Figure 2c are not necessarily composed primarily of weakly bound solvent adducts which result from incomplete desolvation during the electrospray process. Rather, $[\text{C}_5\text{H}_5\text{Ru}(\text{CH}_3\text{CN})_3]^+$ has 18 valence electrons, which can offer it improved stability relative to Cp_2Ru^+ . In fact, $[\text{CpRu}(\text{CH}_3\text{CN})_3]^+[\text{PF}_6]^-$ and $[\text{CpRu}$

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$(\text{CH}_3\text{CN})_3]^+[\text{BF}_4]^-$ salts have been isolated as useful precursors in the synthesis of complexes of even higher stability containing the CpRu group.^{58,59} Under CID conditions (skimmer-collimator voltage difference = 17 V), $\text{Ru-CH}_3\text{-CN}$ bonds can be broken, lowering the abundance of $[\text{CpRu}(\text{CH}_3\text{CN})_3]^+$ in Figure 2c.

Nucleophilic Addition Reactions. Another significant finding is that in several cases, *anionic* groups originating from the solvent were incorporated into the organometallic complex, yet *cationic* species were still observed by ESMS. This includes peaks corresponding to chloride ion addition ($[\text{Cp}_2\text{RuCl}]^+$ from ruthenocene solutions, Figure 5a, and $[\text{Cp}_2\text{OsCl}]^+$ from osmocene solutions, Figure 5b), whose identities were verified by the presence of the predicted isotope distribution patterns when methylene chloride was used as the solvent. Furthermore, $[\text{Cp}_2\text{Os} + \text{trifluoroacetate}]^+$ was observed (Figure 5b) when 0.05–1.0% trifluoroacetic acid was added to the solution. Unexpectedly, $[\text{Cp}_2\text{OsOH}]^+$ was observed when CH_3CN was used as the solvent; OH^- might arise from trace impurities (e.g., water) in the CH_3CN solvent. These reported ions all represent Ru(IV) and Os(IV) species. No ions representing Fe(IV) complexes were observed by ESMS. This is consistent with the inability to form stable or metastable iron chloride or hydroxide complexes by wet chemical methods,⁶⁰ although the iron hydride (Cp_2FeH) has been observed.⁵⁰

It is known that second and third row metallocenes, which do not comply with the 18-electron rule, are quite reactive and difficult to isolate.⁵⁰ For example, Cp_2Re (17 valence electrons) and Cp_2Re^+ (16 valence electrons) are unstable, but Cp_2ReH (18 valence electrons) is quite stable. Rutheninium and osmium ions are not stable in solution as monomers. $[\text{Cp}_2\text{Os}]^+$ exists as a diamagnetic dimer containing an Os-Os bond (2.99 Å).⁶¹ These linked $[\text{Cp}_2\text{M}]^+$ ions are prone toward disproportionation to form Cp_2M and $[\text{Cp}_2\text{M}(\text{IV})]^{2+}$.^{46,52} Like most other high oxidation state metal ions, the latter is a strong Lewis acid. It lacks solution-phase stability, and it is very susceptible to addition reactions with nucleophiles (e.g., Cl^- , OH^-) that may be present in the solvent. Mann and co-workers⁶² have found Cp_2Ru^+ to disproportionate in the presence of weakly coordinating ligands. In addition to the disproportionation process, conceivably some $[\text{Cp}_2\text{M}]^{2+}$ could be formed by electrochemical oxidation.

Anion additions to osmocene have been documented in the literature, including the formation of $[\text{Cp}_2\text{OsI}]^+[\text{PF}_6]^-$ using iodine in acid and of $[\text{Cp}_2\text{OsOH}]^+[\text{PF}_6]^-$ using acidic (aqueous) Fe^{3+} .⁶³ Similarly, oxidation of ruthenocene in the presence of FeCl_3 in ether yielded $[\text{Cp}_2\text{RuCl}]^+[\text{FeCl}_4]^-$ and of ruthenocene in the presence of Br_2 in benzene produced $[\text{Cp}_2\text{RuBr}]^+[\text{Br}_3]^-$.⁴⁶ Results from these studies indicated that the "free cations" Cp_2Ru^+ , $\text{Cp}_2\text{Ru}^{2+}$, Cp_2Os^+ , and $\text{Cp}_2\text{Os}^{2+}$ were unstable in solution. This is consistent with several of our findings, including those given in Table 1 which point to poor detectability of the singly-charged species Cp_2Ru^+

and Cp_2Os^+ (+3 oxidation states) and no detection of the doubly-charged ions $\text{Cp}_2\text{Ru}^{2+}$ and $\text{Cp}_2\text{Os}^{2+}$ (+4 oxidation states). By entering the inner coordination sphere, nucleophilic anions stabilized metal cations having the formal +4 oxidation state. The resulting singly-charged complexes were readily detected by ESMS as shown in Figure 5, parts a and b, and Figure 2d. $\text{Cp}_2\text{Os}^{2+}$ was so reactive that even the weakly nucleophilic trifluoroacetate anion underwent nucleophilic addition, forming a low intensity $[\text{Cp}_2\text{OsOOCF}_3]^+$ ion in the presence of 0.05–1.0% TFA (Figure 5b).

CONCLUSIONS

Organometallic salts dissolved in polar organic solvents (intermediate conductivity) exhibited excellent ESMS characteristics. In the absence of CID, the cations of the salts with characteristic isotope distribution patterns were displayed exclusively. The electrospray instrument can also readily produce ionized forms of metallocene species. A one-electron electrochemical oxidation mechanism is responsible for the formation of intact molecular cations. The stability of the molecular cation is very important in determining the types of ions that will arrive at the MS detector, the intensity of the respective signals, and the influence of the solvent medium. The electrospray instrument produces higher abundance intact molecular cations from compounds which have relatively low $E_{1/2}(\text{ox})$ and IE values [e.g., $E_{1/2}(\text{ox}) < 1.0$ V vs SCE, and $\text{IE} < 8.0$ eV]. Stable oxidized metallocenes can be readily detected, while abundances of less stable species can be augmented via the use of amenable solvents (e.g., CH_3CN or CH_2Cl_2). The ES mass spectrum of decamethylferrocene (Figure 2a) obtained under CID conditions bears many similarities to the EI spectrum.²² The unique isotope distribution patterns of the coordinating metals allow rapid identification of mass spectral peaks attributable to complexes of specific metals without accurate mass measurements.

For those compounds with higher $E_{1/2}(\text{ox})$ or higher IE values, or those whose oxidized forms are very unstable, such as Cp_2Ru and Cp_2Os , ESMS may not produce abundant intact molecular cations. In these cases, protonated molecules may be produced, as may other products of reaction with the solvent and additives. ESMS may thus be used to study characteristics of electrochemical oxidation processes, including products of lower stability, and nucleophilic addition reactions. Solution-phase reactions, of course, are much more difficult to study using other mass spectrometric ionization techniques. Future applications to a wide variety of determinations of organometallic species in polar organic media, and eventually aqueous (including biological) systems, appear very promising.

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