

Synthetic and Mechanistic Aspects of a New Method for Ruthenium-Metalation of Porphyrins and Schiff-Bases

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A new method is presented for metalation of a wide range of free-base, neutral, cationic, and anionic porphyrins in refluxing dimethylformamide (DMF) using an easily prepared $[\text{Ru}(\text{DMF})_6](\text{OTf})_3$ complex, and comparisons are made with the more familiar metalation procedure using $\text{Ru}_3(\text{CO})_{12}$. Both procedures generate $\text{Ru}^{\text{II}}(\text{porp})(\text{CO})\text{L}$ complexes (L = solvent); use of the Ru^{III} -triflate precursor gives yields comparable to, or greater than, those obtained with the carbonyl, and generates no Ru-chlorin impurities. Mechanistic studies on the meso-tetraphenylporphyrin system reveal that the DMF furnishes the CO, which in the presence of essential water reduces the metal, and metalation likely occurs via a $\text{Ru}^{\text{II}}\text{--CO}$ species. Corresponding metalation of tetradentate Schiff-bases gives *trans*- $[\text{Ru}^{\text{III}}(\text{Schiff-base})(\text{DMF})_2]\text{OTf}$ complexes in yields of ~50%, a limitation being the accompanying hydrolysis of the Schiff-base through the presence of trace water.

Introduction

Ruthenium porphyrins continue to reveal rich and diverse chemistry, for example, as biomimetic models,^{1,2} homoge-

neous and supported catalysts (especially for oxidations),^{2,3} synthons within coordination and organometallic chemis-

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try,⁴⁻⁷ building blocks for supra- or supermolecular assemblies,^{7,8} materials,⁹ and sensors,⁴ and in medicinal chemistry.¹⁰ Compared to Fe-porphyrins, the range of Ru-porphyrin systems studied is limited, the field being dominated by “Ru(OEP)”, “Ru(TPP)”, “Ru(TMP)” and “Ru(T-o,o’Cl₂-PP)” derivatives (Scheme 1). In part, this likely results from the limited synthetic methods for insertion of Ru into the macrocycle, especially on comparison with the many metalation methods developed for first-row transition metals.^{5,11}

The first Ru-porphyrin was reported in 1969, metalation being accomplished by refluxing an ethanol solution of RuCl₃¹² under a CO atmosphere, although the Ru^{III}(porp)(CO)Cl formulation of the product was incorrect;¹³ the product was, in fact, a solvated Ru^{II}(porp)(CO) species, as shown shortly afterward when Ru₃(CO)₁₂ and [Ru(CO)₃Cl₂]₂ were used as precursors.¹⁴

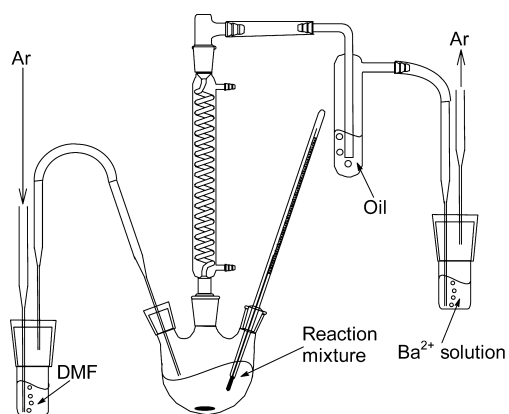
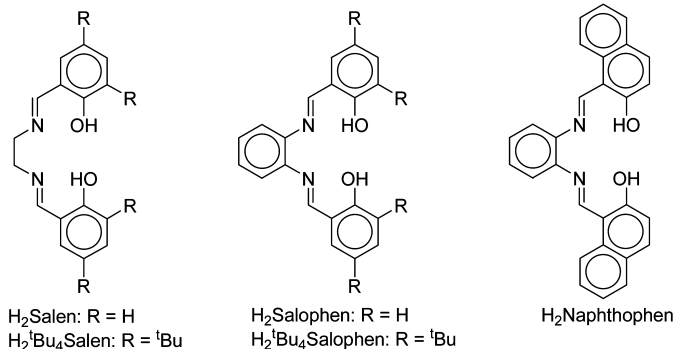
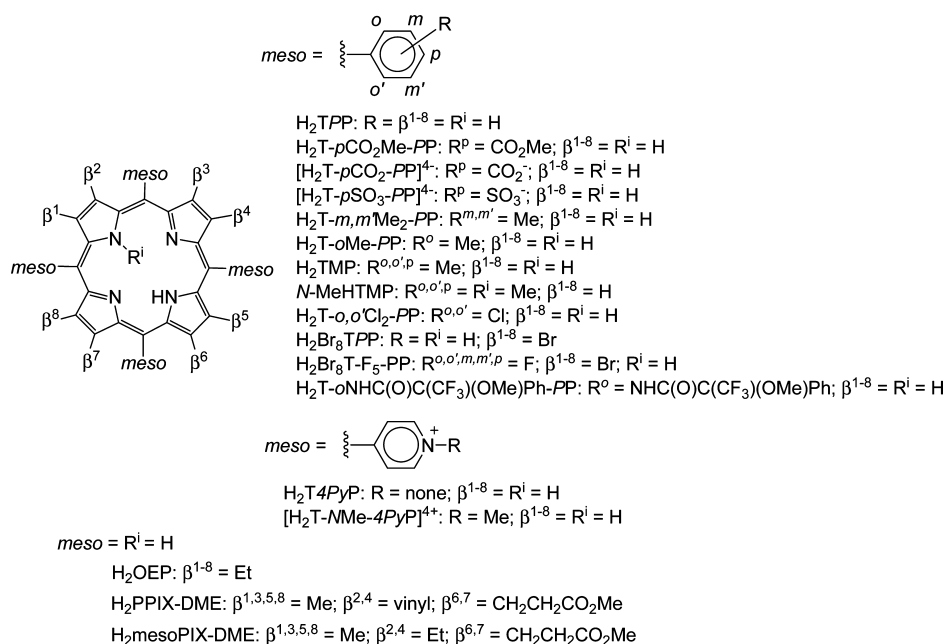
Subsequent Ru-metalations have generally been minor variations of these procedures, including the use of formaldehyde as a source of CO.¹⁵

The popular choice of Ru₃(CO)₁₂ for metalation of porphyrins results from the air-stable carbonyl being available commercially but, because of its price, the dodecacarbonyl is commonly prepared in-house via reduction of precursors such as RuCl₃, RuO₂, or [Ru₃(O)(OAc)₆(H₂O)₃]OAc using CO at 1 atm or high pressure.¹⁶ In these methods, the toxicity of CO^{17c} and possible formation of highly toxic phosgene^{16d,17a} raise safety concerns; indeed, two fatal accidents have occurred via open-air, CO poisoning.^{17b} Within the Ru₃(CO)₁₂ systems, general yield comparisons are difficult. For example, metalation yields for Ru(TMP)(CO)¹⁸ and Ru(T-o,o’Cl₂-PP)(CO)^{6c} are higher when the carbonyl is added portion-wise (81–84%) versus a single addition (25–44%). Of note, the Ru/porphyrin stoichiometry is always > 1, usually 9:1. The choice of solvent is also crucial: a lower boiling point alcohol such as EtOH requires longer refluxing time (~24 h)¹³ than 2-(2'-methoxyethoxy)ethanol (3–5 h),^{6a} although an overnight reaction time has been reported using this solvent.¹⁹ Similarly, refluxing in benzene^{14b,20} requires days, while use of decalin^{6c,11b,21,22} or dimethylformamide (DMF)^{10c,23} can reduce this to hours; a 1–3 week reaction time was reported for metalation of Na₄[H₂(T-pSO₃-PP)] in DMF,^{23a} but details (e.g., concentrations of Ru₃(CO)₁₂ and porphyrin) were not given, and others showed later that this metalation is complete in 4 h when using a 3:1 Ru/porphyrin molar ratio.²⁴ Additives such as bis(triphenylphosphine)iminium chloride^{10c,25} or 2,4,6-trimethylpyridine^{10c} are reported to be beneficial in certain cases. Ruthenium metalations of neutral,

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Scheme 1. Porphyrins and Schiff-Bases Relevant to This Work

Figure 1. Experimental setup for studying Ru-metalation of H_2TTPP .

synthetic porphyrins such as *meso*-tetraaryl- and *meso*-tetraalkylporphyrins, and H_2OEP , typically require subsequent removal of a “Ru-chlorin”,^{6a,21} usually via oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone DDQ.^{6a,19,26} Chromatographic separation of Ru-porphyrinoid compounds is laborious,²¹ and reported yields of $Ru(\text{porp})(CO)$ range from 20 to 60%.^{6a,19,26} Yield reproducibility is an issue when using the $Ru_3(CO)_{12}$ method, although this has provided an entry to all classes of Ru-porphyrins: natural, synthetic, neutral, and charged, within so-called first, second, or third generation compounds.^{11b}

In this paper we report a novel Ru-porphyrin metalation method, which uses the air-stable $[Ru(DMF)_6](OTf)_3$ as metal carrier, and refluxing DMF as solvent and CO source to generate some $Ru^{II}(\text{porp})(CO)$ compounds in good, reproducible yields; further, no Ru-chlorins are detected. Mechanistic studies on the metalation are also presented. Additionally, we show here that the methodology may be adapted to metalation of Schiff-bases.

The literature on Ru-Schiff-base chemistry is less extensive than that of Ru-porphyrins but has flourished since the late 1990s; studies on coordination chemistry and small-molecule chemistry²⁷ have expanded to interest, for example, in homogeneous/heterogeneous/asymmetric catalysis,^{2d,28} photochemistry and NO-chemistry,^{28m,29,30} materials chemistry,^{8f,30} and medicinal chemistry.^{30,31} Metalosalen complexes, with their dianionic $[N_2O_2]$ donor set, are easier to prepare and purify than are the dianionic $[N_4]$ donor-metallporphyrins to which they are often compared.³² Metal precursors have again included $Ru_3(CO)_{12}$,^{27a,d} $RuCl_3 \cdot (NO) \cdot 3H_2O$,^{28b} and $RuCl_2(PPh_3)_3$,^{27b} when the π -acceptor ligands (CO, NO, and PPh_3) are retained in the Ru(Schiff-base) product; these species have been used as catalyst precursors but require initial photolabilization of the π -ac-

ceptor ligands.^{28h,i} The precursor $K_2[RuCl_5(H_2O)]$ has been used to prepare $K[RuCl_2(\text{Schiff-base})]$ derivatives,^{27e-h} while attempted reactions with the common precursors, $RuCl_3$, *cis*- $RuCl_2(\text{MeCN})_4$, and *cis*- $RuCl_2(\text{DMSO})_4$ were unsuccessful.^{27c} The presence of chloride ligand in $Ru(\text{Schiff-base})$ catalysts has been reported undesirable for the asymmetric oxidation of diols²⁸ⁱ and epoxidation of cyclohexene.³³

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The complex $[RuCl_2(p\text{-cymene})]_2$ has been used with chiral Schiff-bases, but the products were not isolated;^{28c} however, subsequent treatment with pyridine generated the substitution-inert $Ru^{II}(\text{Schiff-base})(py)_2$ derivatives that catalyze cyclopropanation of olefins;^{28f} these appear to be the first such complexes containing no chlorides or the π -acceptor ancillary ligands listed above. The direct preparation of π -acceptor-free and chloride-free Ru Schiff-base complexes appeared challenging and led us to test (with some success) the use of $[Ru(\text{DMF})_6](\text{OTf})_3$ for the metalation.

The use of $[Ru(\text{DMF})_6](\text{OTf})_3$ was motivated by a report, describing a simple, one-pot, two-step procedure for its synthesis from $RuCl_3$,^{34c} following earlier literature syntheses via $[Ru(\text{DMF})_6]^{2+}$ species.^{34a,b} The Ru^{III} complex was first used in macrocyclic chemistry to synthesize encapsulated Ru complexes^{34b} and, more recently, homoleptic compounds containing, for example, imidazoles,^{35a} phosphines, arsines, and stilbines,^{35b} and selenoethers and telluroethers.^{35c} Our studies described here represent a contribution to the revival of $[Ru(\text{DMF})_6](\text{OTf})_3$ as a convenient Ru -source in macrocyclic chemistry. Scheme 1 shows the structure and their abbreviations for all of the porphyrin and Schiff-base systems discussed in this Paper.

Experimental Section

General Information. The yellow $[Ru(\text{DMF})_6](\text{OTf})_3$ complex (**1**), prepared by a literature procedure,^{34c} is indefinitely stable if kept in the dark at room temperature (rt, $\sim 20^\circ\text{C}$) under static vacuum in a desiccator; when not stored properly, however, slow decomposition generates a brownish gum impurity, which can be removed by recrystallizing the sample from 2:1 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$. AgOTf , prepared via modification of a literature method (Ag_2O being replaced with Ag_2CO_3),³⁶ was stored under dynamic vacuum in the dark. $\text{H}_2\text{MesoPIX-DME}$ was prepared by H_2 -hydrogenation of $\text{H}_2\text{PPIX-DME}$ (Midcentury).³⁷ N -Methylation of H_2TMP was carried out by a literature procedure³⁸ to yield N -MeHTMP. H_2OEP was a gift from Dr. D. Dolphin. Alkylation of $\text{H}_2\text{T4PyP}$ (Aldrich) with MeOTf ³⁹ afforded $[\text{H}_2\text{T-Me-4PyP}](\text{OTf})_4$ and the tetrachloride was prepared by percolation through a ion-exchange column (Dowex 2×8 , Cl^- form; MeOH as eluent). $\text{H}_2\text{Br}_8\text{TPP}^{40}$ and $\text{Na}_4[\text{H}_2(\text{T-}p\text{SO}_3\text{-PP})]^{41}$ were prepared by literature methods. Other free-base porphyrins were prepared by acid-catalyzed condensation

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of pyrrole and the appropriate aldehyde using literature protocols;⁴² free-base chlorins (if present) were eliminated either oxidatively^{43a,b} or chromatographically.^{43c} Schiff-bases were made via condensation of a diamine and a salicylaldehyde derivative as described elsewhere: H₂Salen,^{44a} H₂Naphthophen,^{44b} H₂Bu₄Salen,^{30a} H₂Bu₄Salophen.^{44c} H₂Salophen (Aldrich) was used as received.

DMF (Fisher Scientific, 0.02% H₂O) and H₂ (Praxair, 99.999%, extra-dry) were used as received; Ar (Praxair, 99.996%) was dried either with Drierite (W.A. Hammond) or with Aquasorb (Mallinckrodt). Gas flow was measured with a Hewlett-Packard soap film flowmeter (HP0101–0113). Distilled H₂O was deoxygenated by saturation with Ar. UV–vis spectra, presented as λ_{max} (log ϵ), were measured at 25 ± 1 °C in quartz cells in a Hewlett-Packard 8452A diode array spectrophotometer. ¹H NMR spectra were recorded on Bruker AV300 or AV400 spectrometers (300.13 and 400.13 MHz, respectively), and referenced to residual solvent protons of *d*₆-DMSO (δ 2.49) or CD₃OD (δ 3.30), TMS-free solvents from Cambridge Isotope Laboratories. IR spectra (KBr, cm⁻¹) were recorded on a Nicolet 4700 FT-IR spectrometer. MS data were collected on a Bruker Esquire ESI ion-trap spectrometer, or on a Kratos Concept III, LSIMS spectrometer using a Cs⁺ gun as ionizing source. Elemental analysis was performed on a Carlo Erba EA 1108 analyzer. Thermal gravimetric analyses were obtained using a TGA 51 Thermogravimetric Analyzer fitted with a quartz furnace tube with a temperature range from ambient to 1200 °C. Stationary phases for column chromatography, neutral, basic, or acidic Al₂O₃ (Fisher Scientific, Brockman activity I, 60–325 mesh) and diatomaceous earth (Fisher Scientific, Celite 545), were used as received. Molar ionic conductance (Λ_{m} , in $\Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$) was determined on a Serfass conductance bridge model RCM15B1 (Arthur H. Thomas Co. Ltd.) connected to a 3404 cell (Yellow Springs Instruments Co.), using a 10⁻³ mol L⁻¹ solution of the complex in DMF at 25 ± 1 °C. Unless otherwise indicated, all solvents and reagents were reagent grade and used as supplied by Aldrich or Fisher Scientific.

In all metalation procedures, a glass pipet and not a stainless steel needle was used to bubble gases into the reaction mixtures.

Metalation of H₂T-*p*-CO₂Me-PP. H₂T-*p*-CO₂Me-PP (20.4 mg, 0.024 mmol), [Ru(DMF)₆](OTf)₃ (**1**), (69.1 mg, 0.070 mmol), and 20 mL of DMF were added to a 3-neck flask equipped with condenser and stir bar. The system was purged with Ar for 15 min at room temperature (rt) and the contents then heated to reflux with stirring under a slow Ar flow (0.88 mL s⁻¹) in the dark for 24 h; the solution gradually changed color from purple to red, and a Ru mirror deposited on the flask wall. The reaction was monitored by UV–vis in acidic medium (HOAc or TFA/CH₂Cl₂ mixtures), when the Soret bands of the free-base (in its protonated form) and Ru(T-*p*-CO₂Me-PP)CO species were well resolved (see Results and Discussion). If the reaction was incomplete and Ru metal was not yet evident, the conversion could be improved by addition of 5–10 μL of deoxygenated H₂O and a further 3–4 h reflux. The resulting solution was concentrated to dryness by rotary evaporation. The residue was suspended in 10 mL of MeOH, the mixture filtered through a Celite pad, and washed with small amounts of MeOH until the washings were clear. The free-base and the Ru-porphyrin were recovered from the Celite by elution with 3:1 CH₂Cl₂/MeCN. The red CH₂Cl₂/MeCN solution was evaporated to dryness, the residue dissolved in 20:1 CH₂Cl₂/MeCN, and purified by column chromatography on neutral Al₂O₃. After the unreacted H₂T-*p*-CO₂Me-PP was eluted (with 20:1 CH₂Cl₂/MeCN), the polarity of the eluent was increased (5:1 CH₂Cl₂/MeCN) and the product fraction was collected; the solvent was removed by evaporation and the resulting purple solid was subsequently dried in an

Abderhalden pistol (H₂O) for ~24 h. The solid was exposed to the atmosphere for ~5 h to give Ru(T-*p*-CO₂Me-PP)(CO)(H₂O). Yield: 19.2 mg (81%). Anal. Calcd for C₅₃H₃₈N₄O₁₀Ru: C, 64.17; H, 3.86; N, 5.65. Found: C, 64.44; H, 4.09; N, 6.05. UV–vis (DMF): 414 nm (5.35), 532 (4.23), 566 (3.54). IR: 3428 (ν_{OH}), 1945 ($\nu_{\text{C=O}}$), 1725 ($\nu_{\text{C=O}}$). ¹H NMR (*d*₆-DMSO): δ 8.56 (s, 8H, β -pyrrole), 8.38–8.21 (m, 16H, *o*- and *m*-C₆H₄CO₂Me), 4.02 (s, 12H, *p*-C₆H₄CO₂CH₃). ESI-MS (9:1 MeOH/CHCl₃, positive mode), M is defined as Ru(T-*p*-CO₂Me-PP)(CO): clusters centered at *m/z* 997 [M + Na]⁺, 975 [M + H]⁺, 946 [M – CO]⁺. ESI-MS (9:1 MeOH/CHCl₃ 1:1, negative mode): *m/z* 1009 [M + Cl]⁻, 981 [M – CO + Cl]⁻. ¹H NMR assignments are based on data for H₂T-*p*-CO₂Me-PP.⁴⁵

Metalation of H₂T-*m,m'*Me₂-PP. The metalation procedure was analogous to the standard one described above, except that H₂T-*m,m'*Me₂-PP (23.7 mg, 0.033 mmol) and **1** (96.4 mg, 0.098 mmol) were used. The Ru-porphyrin retained in the Celite was washed with small portions of MeOH, and recovered with 9:1 CH₂Cl₂/MeCN. The collected red solution was then evaporated to dryness. The resulting solid was dissolved in CH₂Cl₂ and the solution was filtered through acidic Al₂O₃, from which the Ru porphyrin red band was eluted with CH₂Cl₂. The solvent of this was removed by evaporation and the purple residue was then treated as above to yield Ru(T-*m,m'*Me₂-PP)(CO)(H₂O). Yield: 21.9 mg (77%). Anal. Calcd for C₅₃H₄₆N₄O₂Ru: C, 73.00; H, 5.32; N, 6.42. Found: C, 72.57; H, 5.48; N, 6.39. UV–vis (DMF): 414 nm (5.42), 532 (4.27), 566 (3.67). IR: 3443 (ν_{OH}), 1945 (ν_{CO}). ¹H NMR (*d*₆-DMSO): δ 8.57 (s, 8H, β -pyrrole), 7.78 (s, 4H, *o*-C₆H₃Me₂), 7.68 (s, 4H, *o*-C₆H₃Me₂), 7.40 (s, 4H, *p*-C₆H₃Me₂), 2.56 (s, 12H, CH₃), 2.55 (s, 12H, CH₃). ESI-MS (1:1 MeOH/CHCl₃, positive mode), M = Ru(T-*m,m'*Me₂-PP)(CO): *m/z* 855 [M + H]⁺, 826 [M – CO]⁺; ESI-MS (1:1 MeOH/CHCl₃, negative mode): *m/z* 889 [M + Cl]⁻. ¹H NMR assignments are based on data for H₂T-*m,m'*Me₂-PP.⁴⁶

Attempted Metalation of H₂T-*o,o'*Cl₂-PP and H₂TMP. Metalations of H₂T-*o,o'*Cl₂-PP and H₂TMP following the standard procedure were unsuccessful; use of 1:1 DMF/1,2-dichlorobenzene as solvent also gave no formation of Ru-porphyrin. UV–vis spectra showed that the free-base remained unchanged.

Metalation of H₂T-*o*Me-PP. The standard metalation procedure was used, but with H₂T-*o*Me-PP (22.4 mg, 0.033 mmol) of a mixture of atropisomers) and **1** (97.4 mg, 0.099 mmol). The product mixture was then evaporated to dryness, the residue suspended in minimum 4:1 MeOH/H₂O, and the suspension then filtered through Celite. The solid was washed with 5 mL of the MeOH/H₂O mixture and recovered from the Celite with CH₂Cl₂. The collected CH₂Cl₂ fraction contained some water, and so the organic phase was separated, and the CH₂Cl₂ removed by evaporation; residual water was removed by dissolving the sample in 20 mL of C₆H₆ and

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evaporating the solution to dryness. The residue was redissolved in C_6H_6 and purified by chromatography on basic Al_2O_3 . After traces of unreacted free-base were collected with C_6H_6 , the Ru-porphyrin was eluted with 9:1 $CH_2Cl_2/MeCN$; the solvent was removed and the resulting purple solid was converted by the described method to a mixture of Ru(*T-o*Me-PP)(CO)(H_2O) atropisomers. Yield: 25.9 mg (93%). Anal. Calcd for $C_{49}H_{38}N_4O_2Ru$: C, 72.13; H, 4.69; N, 6.87. Found: C, 72.33; H, 4.79; N, 7.22. UV-vis (DMF): 412 nm (5.41), 532 (4.29), 562 (3.42). IR: 3435 (ν_{OH}), 1946 (ν_{CO}). 1H NMR (d_6 -DMSO): δ 8.36, 8.35, 8.34, 8.33 (4 s, 8H, β -pyrrole), 8.06–7.87 (m, 4H, *o*- C_6H_4Me), 7.71–7.55 (m, 12H, *m*- and *p*- C_6H_4Me), 2.02, 2.01, 2.00, 1.96, 1.91 (5 br s, 12H, *o*- $C_6H_4CH_3$). ESI-MS (1:1 MeOH: $CHCl_3$, positive mode), $M = Ru(T-oMe-PP)(CO)$: m/z 821 $[M + Na]^+$, 770 $[M - CO]^+$. 1H NMR and UV-vis data are in agreement with those previously reported for complexes containing the Ru(*T-o*Me-PP)(CO) moiety.^{47a}

Metalation of *N*-MeHTMP. The standard procedure, when applied to *N*-MeHTMP, gave low conversion of the free-base (<20%). The DMF solution of *N*-MeHTMP changed to green upon addition of **1** and remained as such, UV-vis spectra being characteristic of protonated *N*-MeHTMP species (see Results and Discussion). As indicated by thin-layer chromatography (TLC) analysis on basic Al_2O_3 , the product composition varied with each attempted synthesis. Most of the TLC spots fluoresced under 356 nm radiation, and all had lower R_f values than that of the starting material; H_2TMP was never observed. A small amount (<5%) containing “Ru(TMP)(CO)” was once isolated, as evidenced by UV-vis data which were comparable to those reported.¹⁸ Increased reaction time and/or Ru load were ineffective.

Metalation of *H*₂mesoPIX-DME. The standard procedure was used with H_2 mesoPIX-DME (17.0 mg, 0.029 mmol) and **1** (90.1 mg, 0.091 mmol). The product mixture was evaporated to dryness, the residue suspended in *n*-pentane, and the suspension then filtered through Celite. The retained Ru-porphyrin was washed with portions of *n*-pentane and recovered with CH_2Cl_2 . The collected purple solution was evaporated to dryness and the residue purified by column chromatography on SiO_2 using 9:1 $CH_2Cl_2/MeCN$. The solvent of the first fraction was removed, and the residue dried and converted by the standard method to Ru(mesoPIX-DME)(CO)(H_2O). Yield: 17.1 mg (81%). Anal. Calcd for Ru(mesoPIX-DME)(CO)(H_2O), $C_{37}H_{42}N_4O_6Ru$: C, 60.07; H, 5.72; N, 7.52. Found: C, 60.10; H, 5.53; N, 7.39. UV-vis (DMF): 394 nm (5.29), 518 (4.10), 548 (4.30). IR: 3471 (ν_{OH}), 1933 ($\nu_{C=O}$), 1736 ($\nu_{C=O}$). 1H NMR (d_6 -DMSO): δ 9.90, 9.89, 9.87, 9.86 (4 s, 4H, *meso-H*), 4.40–4.18 (m, 4H, $CH_2CH_2CO_2CH_3$), 3.98 (q, 4H, $^3J_{HH} = 7.46$ Hz, CH_2CH_3), 3.55, 3.53 (2 s, 12H, CH_3), 3.52 (s, 6H, $CH_2CH_2CO_2CH_3$), 3.26 (m, 4H, $CH_2CH_2CO_2CH_3$), 1.81 (t, 6H, $^3J_{HH} = 7.46$ Hz, CH_2CH_3). ESI-MS (9:1 MeOH/ CH_2Cl_2 , positive mode), $M = Ru(mesoPIX-DME)(CO)$: m/z 745 $[M + Na]^+$, 722 $[M]^+$, 695 $[M - CO + H]^+$; ESI-MS (9:1 MeOH/ CH_2Cl_2 , negative mode): m/z 753 $[M + MeO]^-$. 1H NMR assignments are based on data for the Ru complex derived from mesoporphyrin IX di-*tert*-butylester;^{1e} UV-vis and IR (ν_{CO}) data agree with those reported for complexes containing the Ru(mesoPIX-DME)(CO) moiety.^{20a}

Metalation of *H*₂PPIX-DME. The procedure used for H_2 mesoPIX-DME, when applied to H_2 PPIX-DME, yielded a complex product mixture, from which Ru(mesoPIX-DME)(CO) was isolated in low yield (<10%). 1H NMR data, particularly a quartet at δ 3.98 and a triplet at δ 1.81 of the CH_2CH_3 group, and MS data for this compound agree with those given in the previous section.

Metalation of H_2Br_8TPP . The standard procedure was used with H_2Br_8TPP (20.0 mg, 0.016 mmol), **1** (51.6 mg, 0.052 mmol), and 15 mL of DMF. The refluxing under Ar was continued for 3 h, when the UV-vis spectrum showed the absence of free-base; the solvent was removed, the residue suspended in MeOH, the mixture filtered through Celite, and the solid washed with MeOH until washings were clear. The Ru-porphyrin was recovered using 4:1 $CH_2Cl_2/MeCN$, and then the solvent was removed. The residue was dissolved in CH_2Cl_2 and purified on a short, SiO_2 column, using CH_2Cl_2 as eluent. The first fraction was collected, mixed with an equal volume of MeCN, and the solution evaporated to dryness to yield Ru(Br_8TPP)(CO)(MeCN). Yield: 3.1 mg (14%). UV-vis (DMF): 434 nm (5.17), 496 (sh), 572 (4.19). IR: 1961 (ν_{CO}). 1H NMR (d_6 -DMSO): δ 8.16–8.11 (m, 4 H, *o*- or *o'*- C_6H_5), 8.05–8.00 (m, 4 H, *o'*- or *o*- C_6H_5), 7.84–7.75 (m, 12 H, *m*- C_6H_5 and *p*- C_6H_5), 2.06 (s, 3 H, CH_3CN). LSIMS, $M = Ru(Br_8TPP)(CO)$: m/z 1374 $[M + H]^+$, 1345 $[M - CO]^+$, 1295 $[M - Br + H]^+$, 1267 $[M - CO - Br + H]^+$.

Metalation of [$H_2T-NMe-4PyP$](OTs)₄. A procedure analogous to the standard one was used with [$H_2T-NMe-4PyP$](OTs)₄ (26.0 mg, 0.020 mmol) and **1** (95.4 mg, 0.097 mmol). The reaction, as monitored by UV-vis after adding a reaction sample to 1 M HCl, was complete after 17 h. The mixture was then evaporated to dryness, the residue washed with Et_2O , dissolved in MeOH and the suspension filtered through Celite. The red solution was concentrated to ~10 mL and filtered through Sephadex G-10. The collected red solution was diluted to 50 mL, run through an anion exchange resin (Bio-Rad AG 1-X2, Cl^- form) to remove some Ru species, and then evaporated to yield a gummy material; this was dissolved in 10 mL of DMF, methyl tosylate (40.9 mg, 0.220 mmol) was added, and the resulting solution was refluxed for 3 h. The solvent was removed, and the residue was washed with dry acetone (8 × 4 mL) in a Schlenk tube for protection against moisture. The resulting solid, mainly [$Ru(T-NMe-4PyP)(CO)$](OTs)₄· xH_2O , was always contaminated with ~15% of the corresponding free-base, as judged by 1H NMR.^{10c} Attempts to produce an analytically pure sample by either recrystallization or chromatography were unsuccessful, as was the use of larger excesses of **1**. Yield: ~15 mg (~40%). ESI-MS (MeOH, positive mode), $M = Ru(T-NMe-4PyP)(CO)$: clusters centered at m/z 574.2 $[M + 2OTs]^{2+}/2$, 325.8 $[M + OTs]^{3+}/3$, 259.4 $[M - CO]^{3+}/3$, 209.6 $[M + MeOH]^{4+}/4$, 201.6 $[M]^{4+}/4$, 194.6 $[M - CO]^{4+}/4$; ESI-MS (MeOH, negative mode): m/z 171 $[OTs]^-$.

Attempted Metalation of [$H_2T-NMe-4PyP$] Cl_4 . The procedure given above for metalation of [$H_2T-NMe-4PyP$](OTs)₄, when applied to the chloride analogue, failed to yield any Ru-porphyrin; UV-vis analysis in aq HCl showed that the free-base remained in solution.

Metalation of $Na_4[H_2T-pSO_3-PP]$. The standard metalation procedure was used with $Na_4[H_2(T-pSO_3-PP)] \cdot 15H_2O$ (210 mg, 0.205 mmol) and **1** (614 mg, 0.622 mmol). After 24 h of reflux, the dark red solution was concentrated to minimal volume, and the product was purified as a purple-red band by chromatography using silica gel with MeOH as eluant. The solvent was removed by evaporation, and the product was collected and dried in vacuo for 1 week. Yield: 133 mg (53%). Anal. Calcd for $Na_4[Ru(T-pSO_3-PP)(CO)] \cdot 4H_2O$, $C_{45}H_{32}N_4O_{17}S_4Na_4Ru$: C, 44.23; H, 2.64; N, 4.58; S, 10.49. Found: C, 44.36; H, 2.70; N, 4.55; S, 10.68. UV-vis (H_2O): 410 nm (5.43), 528 (4.21). IR: 3460 (ν_{OH}), 1923 (ν_{CO}). 1H NMR (CD_3OD): δ 8.65, 8.60 (2 s, 8H, β -pyrrole), 8.25 (m, 16H, *m*- $C_6H_4SO_3^-$ and *o*- $C_6H_4SO_3^-$). TGA: Calcd loss of $4H_2O$: 5.9%. Found: 5.1% (from ~35 to ~60 °C). The 1H NMR, IR (ν_{CO}), and UV-vis data are consistent with those previously reported for the

Ru(*T*-*p*SO₃-*PP*)(CO)⁴⁻ moiety.^{10c,23a,b} EI and LSIMS data showed no parent peak or other peaks related to the title compound.

Metalation of H₂OEP. The standard procedure was used with H₂(OEP) (60 mg, 0.11 mmol), **1** (312 mg, 0.316 mmol), and DMF (30 mL), and a reaction time of 6 h. The product was purified by chromatography using neutral alumina with CH₂Cl₂ as eluent for unreacted H₂(OEP), and with 10% THF/MeOH as eluent for the product. Red, X-ray quality crystals of Ru(OEP)(CO)(THF) were obtained from slow evaporation of a saturated solution of the complex in 10% THF/toluene. Yield: 45 mg (56%). Anal. Calcd for C₄₁H₅₂N₄O₂Ru: C, 67.09; H, 7.14; N, 7.63. Found: C, 66.51; H, 7.17; N, 8.40. UV-vis (DMF): 396 nm (5.63), 518 (4.49), 548 (4.76). IR: 1925 (ν_{CO}). A sample was converted by the standard procedure to give Ru(OEP)(CO)(H₂O). ¹H NMR (*d*₆-DMSO): δ 9.88 (s, 4H, *meso*-H), 4.06–3.93 (m, 16H, CH₂CH₃), 1.86 (t, 24H, CH₂CH₃). LSIMS, M = Ru(OEP)(CO): *m/z* 662 [M]⁺ and 634 [M – CO]⁺. The ¹H NMR, IR (ν_{CO}), and UV-vis spectroscopic data are consistent with those previously reported for the Ru(OEP)(CO) moiety.^{1a,g,6a,20c,47b}

Mechanistic Studies with Metalation of H₂TPP. This metalation was studied in more detail using the apparatus shown in Figure 1, to gain insight into the mechanism. In experiments A–C, the Ar flow was 0.88 mL s⁻¹. Reactions were monitored by withdrawing samples (~50 μL) via a syringe and quenching them by cooling to rt; 2 μL of the sample were transferred to a 1 cm quartz cell, diluted with 1.0 mL of glacial HOAc, and the UV-vis spectrum then recorded. A solution of BaCl₂ (1.00 g in 10 mL of 0.85 M NH₄OH) was used to follow qualitatively any CO₂ evolution;⁴⁸ any precipitated BaCO₃ was filtered off, washed with MeOH, dried in an Abderhalden pistol overnight (EtOH), and characterized by elemental analysis. Control experiments showed no formation of BaCO₃ until [Ru(DMF)₆](OTf)₃ (**1**) was introduced into the system. Use of cold water (~5 °C) in the condenser, and Ar presaturated with DMF at rt, limited evaporation of reaction solvent to ~25% loss over 24 h.

Expt. A. Using H₂TPP (20.0 mg, 0.033 mmol) and DMF (20 mL), the system was purged with Ar for 15 min at rt. The solution was then heated to reflux (153 °C). After 15 min, the thermometer septum was removed, and **1** (95.7 mg, 0.097 mmol) added at time zero, and the system was resealed; samples were then analyzed by UV-vis spectroscopy. After 10.5 h, no Ru metal was observed, and 10 μL (0.556 mmol) of degassed H₂O was then added; after 32 h, metal was observed on the flask walls, and the mixture was worked-up as described for the H₂T-*p*CO₂Me-*PP* system. Yield 23.7 mg (96%) of Ru(TPP)(CO)(H₂O). Anal. Calcd for C₄₅H₃₀N₄O₂Ru: C, 71.13; H, 3.98; N, 7.37. Found: C, 70.65; H, 4.31; N, 7.10. UV-vis (DMF): 412 nm (5.60), 532 (4.72). IR: 3412 (ν_{OH}), 1946 (ν_{CO}). ¹H NMR (*d*₆-DMSO) δ 8.55 (s, 8H, β-pyrrole), 8.20–8.17 (m, 4H, *o*- or *o'*-C₆H₅), 8.08–8.04 (m, 4H, *o'*- or *o*-C₆H₅), 7.80–7.73 (m, 12 H, *m*-C₆H₅ and *p*-C₆H₅). LSIMS, M = Ru(TPP)(CO): *m/z* 742 [M]⁺, 714 [M – CO]⁺. The ¹H NMR, IR (ν_{CO}) and UV-vis data agree with reported data for complexes containing Ru(TPP)(CO).^{6g,14a,20a,b,d,21} Structural analysis of X-ray quality red crystals, obtained by slow evaporation of a saturated solution of the aqua complex in 5% pyridine/benzene, showed the molecule

to be Ru(TPP)(CO)(py), identical to that reported in 1973.⁴⁹ The BaCO₃ (12.2 mg, 0.062 mmol) was isolated; (Anal. Calcd. C, 6.06. Found: C, 6.28).

Expt. B. The procedure was identical to that described in Expt. A, except that at time zero deoxygenated H₂O (200 μL, 11.1 mmol) was added. After 2.5 h, Ru metal was evident, and no further metalation was seen. Work-up yielded 16.8 mg (68%) of Ru(TPP)(CO)(H₂O); 1.1 mg (5%) of unreacted H₂TPP was recovered from the neutral Al₂O₃ chromatography column.

Expt. C. DMF alone (20 mL) was used and the solvent was purged with Ar for 15 min at rt, prior to being refluxed. After 15 min, **1** (96.3 mg, 0.098 mmol) was added (time zero), and the system was sealed and samples taken subsequently. After 2 h, H₂TPP (20.4 mg, 0.033 mmol) was added. The reaction was monitored for 7 h, when workup yielded 15.2 mg (60%) of Ru(TPP)(CO)(H₂O) and 5.9 mg (29%) of H₂TPP.

Metalation of H₂'Bu₄Salen. A mixture of H₂'Bu₄Salen (10.0 mg, 0.020 mmol) and **1** (60.1 mg, 0.061 mmol) in 10 mL of DMF was refluxed for 3 h under air, protected from moisture (using Drierite) and light (Al foil); the reaction was monitored by TLC (SiO₂, 10:1 CH₂Cl₂:EtOH). The mixture was then concentrated to an oily residue, and purified on SiO₂, using 10:1 CH₂Cl₂:EtOH as eluent; the blue band was collected, and the solution evaporated to dryness. The product was dried in an Abderhalden pistol (EtOH) overnight. Yield of [Ru('Bu₄Salen)(DMF)₂](OTf): 7.8 mg (44%). Anal. Calcd. for C₃₉H₆₀F₃N₄O₇RuS: C, 52.81; H, 6.82; N, 6.31. Found: C, 52.91; H, 6.87; N, 6.06. UV-vis (DMF): 368 nm (4.28), 516 (3.36), 706 (3.71). IR: 1638 (ν_{CO}), 1267 (ν_{SO₃}), 1031 (ν_{CF₃}). Λ_M (DMF): 67 Ω⁻¹ mol⁻¹ cm². ESI-MS (1:1 CH₂Cl₂/MeOH, positive mode), M = Ru('Bu₄Salen)(DMF)₂: *m/z* 738 [M]⁺, 592 [M – 2DMF]⁺. ESI-MS (1:1 CH₂Cl₂/MeOH, negative mode): *m/z* 662 [M – 2DMF + 2Cl]⁻, 149 [OTf]⁻.

Metalation of H₂'Bu₄Salophen. The procedure used was as given for H₂'Bu₄Salen, but using H₂'Bu₄Salophen (10.9 mg, 0.020 mmol). A resulting green band on the silica gel was collected, and the solution was evaporated to dryness, the product again being similarly dried overnight. Yield of [Ru('Bu₄Salophen)(DMF)₂](OTf)·½H₂O: 10.6 mg (57%). Anal. Calcd. For C₄₃H₆₁F₃N₄O_{7.5}RuS: C, 54.70; H, 6.51; N, 5.93. Found: C, 54.82; H, 6.60; N, 5.83. UV-vis (DMF): 300 nm (4.38), 312 (sh), 344 (sh), 376 (sh), 430 (4.32), 576 (sh), 612 (sh), 830 (3.50). IR: 1637 (ν_{CO}), 1268 (ν_{SO₃}), 1031 (ν_{CF₃}). Λ_M (DMF): 65 Ω⁻¹ mol⁻¹ cm². ESI-MS (MeOH, positive mode), M = [Ru('Bu₄Salophen)(DMF)₂]: *m/z* 787 [M]⁺, 641 [M – 2DMF]⁺. ESI-MS (MeOH, negative mode): 149 [OTf]⁻.

Attempted Metalation of H₂Salen, H₂Salophen, and H₂Naphthophen. The procedure described for H₂'Bu₄Salen, when tried for H₂Salen, H₂Salophen, or H₂Naphthophen, yielded intractable product mixtures. Attempts to isolate pure compounds by recrystallization or chromatography were unsuccessful, although MS data of the product mixtures showed that metalation did occur.

Results and Discussion

Ru-Metalation of Porphyrins. The new protocol for metalation of porphyrins with [Ru(DMF)₆](OTf)₃ was approached in a way to provide insight into the underlying chemistry. Table 1 summarizes characteristics of the porphyrins studied and, in the case of successful metalations, presents the yield of isolated product, which, with few exceptions, was formulated as Ru(porp)(CO)(H₂O); these

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Table 1. Porphyrins Studied for Metalation by [Ru(DMF)₆](OTf)₃, and Yields of Ru-Carbonyl

porphyrin	substituents		aryl-substituents				porphyrin charge			% yield ^a
	<i>meso</i> -	β -	<i>p</i> -	<i>m,m'</i> -	<i>o</i> -	<i>o,o'</i> -	neutral	anionic	cationic	
H ₂ TPP	+	–	–	–	–	–	+	–	–	96
H ₂ T- <i>p</i> CO ₂ Me-PP	+	–	+	–	–	–	+	–	–	81
H ₂ T- <i>m,m'</i> Me ₂ -PP	+	–	–	+	–	–	+	–	–	77
H ₂ TMP	+	–	+	–	–	+	+	–	–	0 ^b
H ₂ T- <i>o,o'</i> Cl ₂ -PP	+	–	–	–	–	+	+	–	–	0 ^b
H ₂ T- <i>o</i> Me-PP	+	–	–	–	+	–	+	–	–	93
<i>N</i> -MeHTMP	+	–	+	–	–	+	+	–	–	0 ^b
H ₂ OEP	–	+	not applicable				+	–	–	56 ^c
H ₂ mesoPIX-DME	–	+	not applicable				+	–	–	81
H ₂ PPIX-DME	–	+	not applicable				+	–	–	<10 ^{d,e}
H ₂ Br ₈ TPP	+	+	–	–	–	–	+	–	–	14 ^{d,f}
Na ₄ [H ₂ (T- <i>p</i> SO ₃ -PP)]	+	–	+	–	–	–	–	+	–	53
[H ₂ T- <i>N</i> Me-4PyP](OTf) ₄	+	–	+	–	–	–	–	–	+	~50 ^d
[H ₂ T- <i>N</i> Me-4PyP]Cl ₄	+	–	+	–	–	–	–	–	+	0 ^b

^a Isolated. ^b Porphyrin free-base unreacted. ^c Recrystallized. ^d See text. ^e Yield refers to Ru(mesoPIX-DME)(CO)(H₂O). ^f H₂Br₈TPP decomposes in refluxing DMF. + Studied.

were characterized by spectroscopic (UV–vis, IR, and ¹H NMR), spectrometric (ESI-MS), and elemental analyses.

General Considerations. (a) Purification. When the reaction product mixture was concentrated to a minimum volume and directly purified by column chromatography (using first an apolar eluent and then a more polar mixture), some loss in Ru porphyrin was observed because residual DMF in the sample modified the polarity of the initial eluent (CH₂Cl₂ or C₆H₆) and resulted in some Ru-porphyrin being eluted in the solvent front, together with unreacted free-base. The purification procedure was improved by introducing a filtration step prior to the chromatography to eliminate the DMF. As neutral free-base porphyrins and Ru-porphyrins are almost insoluble in MeOH and H₂O, the rotovap-concentrated product mixture was suspended in MeOH or MeOH/H₂O and filtered through Celite; the solid (unreacted free-base, Ru-porphyrin, and Ru-metal) was washed with the polar medium, and this eliminated residual DMF and some brownish, uncharacterized Ru species (nonporphyrinic as indicated by UV–vis spectra). The free-base and the Ru-porphyrin were then extracted from the Celite with CH₂Cl₂, and purified using an Al₂O₃ column (on which the Ru-porphyrins were strongly adsorbed) using as eluents initially CH₂Cl₂ (to collect the unreacted free-base) and then CH₂Cl₂/MeCN mixtures (to recover the Ru-porphyrin). For the metalation of H₂TPP, for example, this modified procedure increased the isolated yield of Ru-porphyrin from 50 to 96%.

(b) UV–vis Spectroscopy. Electronic spectroscopy is valuable for monitoring metalation reactions and checking product purity. A typical porphyrin shows an intense Soret band ($\epsilon \sim 10^5 \text{ M}^{-1} \text{ cm}^{-1}$) in the 350–450 nm region and four weaker bands ($\epsilon \sim 10^3\text{--}10^4$) in the 450–800 nm region; metalation increases the local symmetry from *D*_{2h} (free-base) to *D*_{4h} (metalloporphyrin) and is accompanied by a collapse in the number of the low-energy bands from 4 to 2 (or even 1).⁵⁰ The Soret band of Ru(porp)(CO) species does not shift appreciably from that of the corresponding free-base under neutral conditions, but the low-energy bands can be used

for following metalation. Because Ru(porp)(CO) compounds are stable under acidic conditions,^{11a} a better way to monitor metalation or detect free-base contamination in isolated Ru(porp)(CO) fractions is to record the spectra in acidic media (e.g., HOAc, TFA, or TFA/CH₂Cl₂), when the free-base is protonated to so-called “dication” species,⁵¹ this referring only to the charges on the porphyrin N₄-core and not those of peripheral substituents. These dications have *D*_{4h} symmetry and electronic spectra that resemble those of Ru(porp)(CO) compounds, but all absorption maxima of the dications are significantly red-shifted, allowing for unambiguous identification of mixtures of unmetallated porphyrin and Ru(porp)(CO) species.

(c) IR Spectroscopy. This was used mainly to characterize Ru(porp)(CO)(H₂O) species by verifying the absence of ν_{NH} of free-base porphyrins ($\sim 3315 \text{ cm}^{-1}$) and confirming the presence of coordinated CO and H₂O ($\nu_{\text{CO}} \sim 1940$, $\nu_{\text{OH}} \sim 3440 \text{ cm}^{-1}$). Other functional-group bands are also reported when present.

(d) ¹H NMR Spectroscopy. Metalation results in the disappearance of the distinct, ring-current shielded signal associated with the free-base, inner core hydrogens (δ about –3).⁵² ¹H NMR spectra were also useful in determining the purity of the isolated complexes, because “grease” ($\delta \sim 0$) and residual workup solvent, the common impurities, could be easily identified.⁵³ The purity of the Ru(porphyrin)(CO) complexes depended on the solvent used in their synthesis. Within Ru(porp)(CO)(L) complexes, the L was difficult to identify when “non-coordinating solvents” such as C₆D₆ or CDCl₃ were used. Because of the *trans*-effect of CO, the usually weak Lewis base L, which is derived from the workup procedure (commonly MeCN, H₂O, MeOH, DMF, or a mixture of these), is typically in fast exchange with

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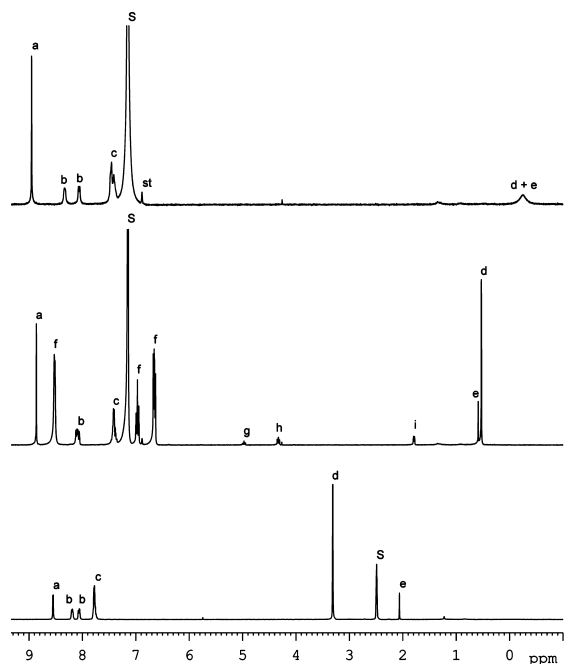


Figure 2. ^1H NMR spectra of crude $\text{Ru}(\text{TPP})(\text{CO})(\text{MeCN})$ in C_6D_6 (top), C_6D_6 + excess pyridine (middle), and d_6 -DMSO (bottom). Assignments: a, β -pyrrole; b, *o*-Ph; c, *m*- and *p*-Ph; d, residual H_2O ; e, MeCN; f, free pyridine; g, γ -pyridine (coord.); h, β -pyridine (coord.); i, α -pyridine (coord.); S, solvent; st, solvent satellite ($\text{H}-^{13}\text{C}$ coupling).

residual water in the deuterated solvent; this yields a broad signal, whose chemical shift is uninformative as it depends on the relative concentrations of water and L (in free and coordinated states) (Figure 2, top). To identify L in C_6D_6 or CDCl_3 solutions, addition of excess pyridine was usually helpful (Figure 2, middle). An easier method for identifying L was to record the ^1H NMR spectrum in d_6 -DMSO (DMSO was not used in any stage of the synthesis), when the spectrum of “ $\text{Ru}(\text{porp})(\text{CO})(\text{L})$ ” corresponds to that of $\text{Ru}(\text{porp})(\text{CO})(d_6\text{-DMSO})$ and free L (Figure 2, bottom). The ^1H assignments were made by comparison with data for the corresponding free-base and/or a literature congener; $\text{Ru}(\text{porp})(\text{CO})(\text{L})$ species lack a horizontal plane of symmetry, and the two faces of the porphyrin ring are inequivalent.

(e) Elemental Analysis. Samples recrystallized from (wet) $\text{MeCN}/\text{CH}_2\text{Cl}_2$ mixtures sometimes contained a mixture of $\text{Ru}(\text{porp})(\text{CO})(\text{MeCN})$ and $\text{Ru}(\text{porp})(\text{CO})(\text{H}_2\text{O})$ as revealed by NMR (in d_6 -DMSO). Although the elemental analysis and ^1H NMR data for these $[\text{Ru}(\text{porp})(\text{CO})(\text{MeCN})]_x$ - $[\text{Ru}(\text{porp})(\text{CO})(\text{H}_2\text{O})]_y$ samples (where $x + y = 1$) were in perfect agreement, such “fractional” formulations could be avoided by converting the samples to $\text{Ru}(\text{porp})(\text{CO})(\text{H}_2\text{O})$ using a modification of a reported procedure:^{14a} the sample was heated at $100\text{ }^\circ\text{C}$ under vacuum for up to 1 day in an Abderhalden pistol (H_2O), during which time coordinated MeCN was eliminated (as revealed by ^1H NMR). The sample was then exposed to the atmosphere for ~ 1 h to “pick up water”, this procedure yielding solids that reproducibly analyzed for $\text{Ru}(\text{porp})(\text{CO})(\text{H}_2\text{O})$.

(f) Avoidance of Stainless-Steel Needles. Contamination by Fe-porphyrins was observed on using stainless-steel needles for bubbling Ar through a reaction mixture. Under

certain conditions, particularly using temperatures just below that of refluxing DMF, Fe-porphyrins, characterized by MS and UV-vis, were the major product; the needles became visibly corroded, consistent with a reported metalation using elemental Fe.⁵⁴ Thus, such needles were replaced with long glass pipettes.

Effects of Peripheral Substituents. The porphyrins were selected for study so that the effects of peripheral substituents on the metalation using $[\text{Ru}(\text{DMF})_6](\text{OTf})_3$ (**1**) could be examined. Noticed was the successful metalation to form $\text{Ru}(\text{TPP})(\text{CO})(\text{H}_2\text{O})$, in contrast to the nonmetalation of H_2TMP . Electronic or steric effects of the *meso*-phenyl substituents must play a role and, particularly because of the intense interest in $\text{Ru}(\text{TMP})(\text{CO})$ derivatives in catalytic oxidations,² studies with a series of *meso*-tetraarylporphyrins, including *para*-, *di-meta*-, *ortho*-, and *di-ortho*-aryl substituents, were undertaken. The $\text{Ru}(\text{T-}p\text{CO}_2\text{Me-PP})(\text{CO})(\text{H}_2\text{O})$ complex was successfully prepared (Table 1), and this *p*-substituted porphyrin was chosen because (i) (carbomethoxy)phenyl-porphyrins are easy to prepare (and are available commercially), (ii) their metal-derivatives are readily purified, hydrolyzed, and ionized to their water-soluble, carboxylato derivatives, and (iii) carboxyporphyrins and their metal complexes are of use in diverse areas of chemistry and biology, including medicinal chemistry,⁵⁵ supramolecular chemistry and materials,⁵⁶ analytical chemistry,⁵⁷ biomimetic catalysis,⁵⁸ and photochemistry.⁵⁹ A $\text{Ru}(\text{T-}p\text{CO}_2\text{Me-PP})(\text{CO})$ derivative has been prepared using $\text{Ru}_3(\text{CO})_{12}$,^{58b} but purification and characterization details were not provided; however, base-hydrolysis to the water-soluble $\text{H}_4[\text{Ru}(\text{T-}p\text{CO}_2\text{PP})(\text{CO})]$ was accomplished in high yield as shown by ^1H NMR, but the nature of the ligand *trans* to CO was not discussed, and is presumably H_2O . This reported synthesis via the ester complex is more convenient than the

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direct, but troublesome, Ru₃(CO)₁₂-metalation of H₄[H₂(T-*p*CO₂-PP)].^{10c} Our metalation of H₂T-*m,m'*Me₂-PP gave the new compound, Ru(T-*m,m'*Me₂-PP)(CO)(H₂O), which may be considered a “converse” Ru(TMP)(CO) derivative. Of note, this new complex was the only one that was purified on acidic Al₂O₃; attempts to find a solvent mixture to separate the complex from its unreacted free-base on SiO₂, and neutral or basic Al₂O₃, were unsuccessful. In acidic Al₂O₃, the free-base is presumably protonated and strongly held by the stationary phase when using an apolar mobile phase. Purification of Ru(T-*m,m'*Me₂-PP)(CO) was thus accomplished by elution with CH₂Cl₂, which left the protonated free-base at the top of the column as a green band that was eluted with 1:1 MeOH/CH₂Cl₂; the pure free-base was subsequently isolated using basic Al₂O₃. The acidic Al₂O₃ approach is novel and could be extended to other neutral Ru-porphyrins, especially in high-yield metalation reactions where the recovery of unreacted free-base is not essential.

The successful metalation of H₂TTPP, H₂T-*p*CO₂Me-PP, and H₂T-*m,m'*Me₂-PP (unsubstituted, *p*-, and *m*-substituted *meso*-tetraphenylporphyrin, respectively) strongly implies that the nonmetalation of H₂TMP is associated with the *o*-phenyl substituents. To probe whether a steric and/or electronic effect was involved, metalation of the di-*ortho*-substituted porphyrin H₂T-*o,o'*Cl₂-PP was chosen because the electron-withdrawing Cl and electron-donating Me groups have similar van der Waals radii.⁶⁰ The attempted metalation of H₂T-*o,o'*Cl₂-PP using **1** was unsuccessful (as for H₂TMP), implying that steric effects are probably more significant—a common feature in the metalation of porphyrins. Kinetic studies on formation of first-row transition metal-porphyrin complexes have established that di-*o*-substituted *meso*-tetraarylporphyrins are the least reactive among various aryl-substitution patterns, and that electronic factors are of minor significance. For example, the relative rates of Zn^{II} incorporation into substituted-H₂TTPP follow the order: *para*- (500) ≥ di-*meta*- (183) > *ortho*- (28) > di-*ortho*- (1).^{11c,61} Further, a study of the *p*-substituted *meso*-tetraphenylporphyrins, H₂T-*p*X-PP (X = Me, H, F, Cl, Br, CF₃, NO₂), showed that electronic effects on the Zn^{II}-metalation rate are generally negligible, with exceptions (a 5- to 20-fold rate increase) seen for X = NH₂, OMe, or OH groups that can donate electron density by resonance into the porphyrin ring.^{11c} The (steric) “*ortho* effect” has been extensively studied, and there is agreement that the rate-limiting step for metalation involves the formation of a transient “sitting atop” (SAT) complex. Although the exact nature of this species remains debatable, the metal is considered to reside on one face of the porphyrin ring, coordinated to one or two pyrrole nitrogens; this forces the remaining nitrogens towards the opposite face, away from the metal, and thus the porphyrin ring is highly deformed.^{11c,61,62} This molecular flexibility of a porphyrin ring, studied by X-ray and theoretical analysis

of diprotonated, metal-free porphyrin species, decreases with the steric bulk of *o*-substituents because of their interaction with the β-pyrrole hydrogens.⁶³ The findings are consistent with kinetic data for metal incorporation into porphyrins.^{11c,61} Our metalation procedure was successful with the mono-*ortho* substituted derivative, H₂T-*o*Me-PP. This porphyrin exists as a mixture of atropisomers (rotational isomers), but no attempt was made to isolate the isomers, as atropisomerization is likely to occur under the refluxing DMF conditions of the metalation; Ru(T-*o*Me-PP)(CO)(H₂O) was isolated as a mixture of atropisomers, in high yield. This finding suggests that the limitation of the [Ru(DMF)₆](OTf)₃ method, with regards to the “*ortho* effect”, is restricted to di-*ortho* substituted *meso*-tetraarylporphyrins, because of the low deformability of these porphyrin rings. Nevertheless, the method is a facile, safe, high-yield process for Ru-metalation of *para*-, (di-)*meta*-, and (mono-)*ortho*-aryl substituted porphyrins.

Difficulty in metallating the di-*ortho* substituted porphyrins, H₂TMP and H₂T-*o,o'*Cl₂-PP, is also reported when using Ru₃(CO)₁₂; harsh conditions using high boiling-point solvents such as decalin or 1,2-dichlorobenzene are required.^{6c,18,64} The high temperature likely overcomes the energy barrier associated with the porphyrin ring deformation. Solvent mixtures (1:1) of DMF with decalin and with 1,2-dichlorobenzene were tried with **1**, but no Ru-porphyrin was observed by UV-vis or TLC; the free-bases were stable under such conditions, but **1** decomposed to a dark precipitate. Faster metalation is needed, as the actual “active” Ru species from the triflate precursor (see below) and from the use of Ru₃(CO)₁₂ decompose to metal under the reaction conditions. Another approach to overcome the “poor deformability problem” of di-*ortho* substituted porphyrins is modification of the porphyrin ring to give a stable, more deformed configuration prior to metalation, for example, by replacing an inner-core hydrogen by Me to yield an *N*-alkylporphyrin, which after metalation could be dealkylated by base.⁶⁵ Indeed, the rate of metalation of *N*-alkylporphyrins, which do model the distorted porphyrin intermediate is 10³–10⁵ times higher than that of the corresponding porphyrins.⁶⁶ However, the attempted metalation of *N*-MeHTMP using **1** generated a green mixture, whose UV-vis spectrum indicated the presence of protonated free-base. *N*-Methylporphyrins are strong bases⁶⁷ and the proton source is likely H₂O, possibly activated by coordination to the Ru; the use

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of dry DMF was not considered because H₂O is needed for successful metalation, see below.

Our metalation method was also successful with H₂OEP and H₂mesoPIX-DME, both neutral, β -octaalkylsubstituted porphyrins. The isolated Ru(OEP)(CO)(THF) was characterized by an X-ray structure (see Figure S1 in the Supporting Information), which is analogous to that of other Ru(OEP)(CO)(L) complexes (e.g., L = H₂O⁶⁸ and various N-donors⁶⁹) and the [Ru(T-*o*NHC(O)C(CF₃)(OMe)Ph-PP)(CO)(THF)]⁴⁺ structure;⁷⁰ all the Ru–C bond lengths are in the range 1.78–1.82 Å, and the Ru–O bond length of 2.241(3) Å in Ru(OEP)(CO)(THF) is close to those in Ru(OEP)(CO)(H₂O) (2.253(2) Å)⁶⁸ and [Ru(T-*o*NHC(O)C(CF₃)(OMe)Ph-PP)(CO)(THF)]⁴⁺ (2.28(1) Å).⁷⁰

The isolated Ru(mesoPIX-DME)(CO)(H₂O) complex provides entry into effective preparation of natural porphyrin complexes of Ru, of interest in biomimetic systems:^{1d,j} derivatives of Ru(mesoPIX-DME)(CO) have been used in the reconstitution of myoglobin^{1b,c} and horseradish peroxidases.^{1h} Attempts to metalate H₂PPIX-DME, the ester of the heme porphyrin, were unsuccessful, most of the free-base being decomposed, presumably via some reaction involving the vinyl groups of H₂PPIX-DME.⁷¹ Nevertheless, a small amount of a Ru(mesoPIX-DME)(CO) derivative was isolated from the product mixture, showing that hydrogenation of the vinyl groups had taken place; the nature of the reduction is unclear. Literature reports on the metalation of H₂PPIX-DME using Ru₃(CO)₁₂ are somewhat contradictory: one report^{1h} states “the protoporphyrin complex was not obtained due to the rigorous synthetic conditions” (referring to refluxing C₆H₆), while another^{1j} claims to have prepared Ru(PPIX-DME)(CO) in refluxing toluene. However, the only characterization given was a ν_{CO} IR stretch, presumably that of a Ru-carbonyl porphyrin, but the nature of the peripheral substituents is uncertain, particularly in reference to the integrity of the vinyl groups.

The new metalation method was tested with fully substituted (dodecasubstituted) porphyrins, of which β -octahalogeno *meso*-tetraarylporphyrins have received intense interest in a quest for robust oxidation catalysts.^{1m,3o,72} Dodecasubstituted porphyrins are highly distorted and, not surprisingly, incorporate metals 10³–10⁵ times faster than planar tetra- or octasubstituted analogues.⁷³ Although β -octahalogeno *meso*-tetraarylporphyrins are reportedly unstable in refluxing

DMF,^{11b,74} H₂Br₈TPP was tested because of its more accessible synthesis than those of β -alkyl or β -aryl *meso*-tetraarylporphyrins. The metalation reaction with the octabromo porphyrin was stopped after 3 h, since UV–vis analysis then revealed the absence of free-base which had been converted to Ru(Br₈TPP)(CO) or destroyed; the complex was isolated in 14% yield and, although low compared to that of H₂TPP (96%), the result is still conceptually attractive. A Ru₃(CO)₁₂-metalation of H₂Br₈T-F₅-PP, involving a 50 h reaction in refluxing benzene, has been reported but no yield was given; longer reaction times led to porphyrin dehalogenation and decomposition.^{20f} Our attempts to metalate H₂Br₈TPP with Ru₃(CO)₁₂ in refluxing decalin yielded no Ru(Br₈TPP)(CO).

Interest in the chemistry of water-soluble metalloporphyrins^{11c} led us to test **1** for metalation of water-soluble porphyrins. The complex Na₄[Ru(T-*p*SO₃-PP)(CO)]·4H₂O, was isolated in 53% yield, the water-content being supported by elemental analysis and by thermogravimetric analysis (TGA), which showed a weight loss corresponding to 3.5H₂O. Incorporation of Ru into [H₂T-*N*Me-4PyP]⁴⁺ was demonstrated, but a cationic Ru-porphyrin could not be isolated pure. The procedure described gave a sample of [Ru(T-*N*Me-4PyP)(CO)](OTs)₄·*x*H₂O contaminated with ~15% of the free-base, as judged by integration of the CH₃ signals in ¹H NMR spectrum. In the procedure, filtration through Celite eliminated Ru metal, and polar, unidentified impurities were removed by percolation through a size-exclusion Sephadex column and a Cl[–]-exchange resin. ¹H NMR analysis at this stage showed that the tosylate anions were exchanged, and ESI-MS data indicated that partial demethylation had occurred; thus, the sample of tetra- and tricationic derivatives were remethylated with MeOTs to yield the final mixture of [Ru(T-*N*Me-4PyP)(CO)]⁴⁺ and [H₂T-*N*Me-4PyP]⁴⁺ as tosylate salts, the chlorides being eliminated as CH₃Cl during reaction with the MeOTs.⁷⁵ Of note, metalation of [H₂T-*N*Me-4PyP](OTs)₄ with MnCl₂ in DMF, also shows instability of the macrocycle.⁷⁶ Use of [H₂T-*N*Me-4PyP]Cl₄ with **1** gave no metalation, demonstrating the significant role of the counterion; presumably, the more strongly coordinating Cl[–] scavenges the Ru and precludes metalation. There is a report on synthesis of a cationic Ru-porphyrin, derived from *meso*-tetrakis(*N*-ethyl-*N,N*-dimethylanilinium-4-yl)porphyrin, by heating the free-base porphyrin with RuCl₃ in water (pH 5) at 80 °C for 30 min, followed by treatment of the crude product with pyridine at 80 °C for another 30 min; the product was formulated as Ru^{II}(porp)(py)₂, but associated counter-ions for the tetracationic Ru(porp) moiety were not mentioned, neither was proof of the assigned oxidation state.⁷⁷

The metalation procedures using [Ru(DMF)₆](OTf)₃ (or Ru₃(CO)₁₂) are likely governed by a balance between

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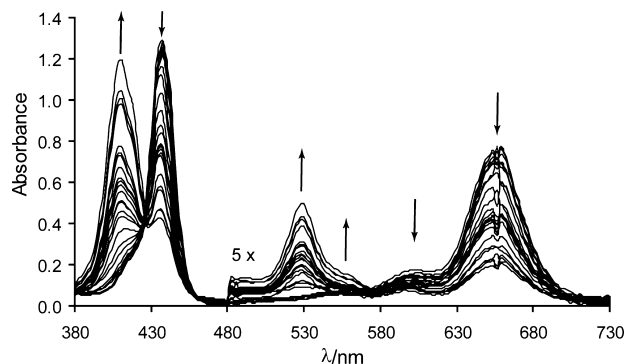


Figure 3. UV-vis spectral changes (in HOAc) over 32 h during metalation of H₂TPP with [Ru(DMF)₆](OTf)₃ (**1**); the 480–730 nm region is expanded 5 times for clarity.

antagonistic processes: decomposition of free-base porphyrin and Ru species (into metal) and insertion of the Ru into the porphyrin.

Mechanistic Aspects. The overall metalation involves at least three distinct steps: reduction of Ru^{III} to Ru^{II}, CO abstraction from the DMF, and Ru incorporation into the macrocycle; the finding that metalation does not occur under air suggests that reduction of Ru is a prerequisite step. Studies on metalation of H₂TPP (Mechanistic Studies, Expts. A–C) provided a reproducible, semiquantitative analysis of the progress of the process. Figure 3 shows typical UV-vis changes during the metalation, the spectra being recorded in glacial HOAc for convenient resolution of the bands of the diprotonated free-base and the metalation product (see General Considerations, (b)). Whether there are real isosbestic points is unclear because of the reduction of the reactant volume with time (~20% over 24 h); any third species such as a SAT intermediate, which might be decomposed in HOAc to diprotonated species, is considered undetectable. Nevertheless, with the protocol used, some fundamental questions about the [Ru(DMF)₆](OTf)₃ method can be addressed.

Carbon monoxide, formed from DMF (eq 1a), can reduce metal ions in solution (eq 1b),



including reduction of Ru(III) to Ru(0),⁷⁸ and is considered to be the reductant in the metalation process: CO₂ was evolved as demonstrated by its conversion to BaCO₃ (reliable 18th century chemistry!⁷⁹). Indeed, CO₂ was detected in successful and unsuccessful metalations, as well as in the absence of porphyrin, implying that the Ru reduction is a porphyrin-independent process. These data do not rule out CO-reduction of a Ru^{III}-porphyrin to a Ru^{II} analogue, but other findings (see below) suggest that Ru^{III} is reduced prior to metalation. Figure 3 shows data for Expt. A under the standard metalation conditions, from which the consumption

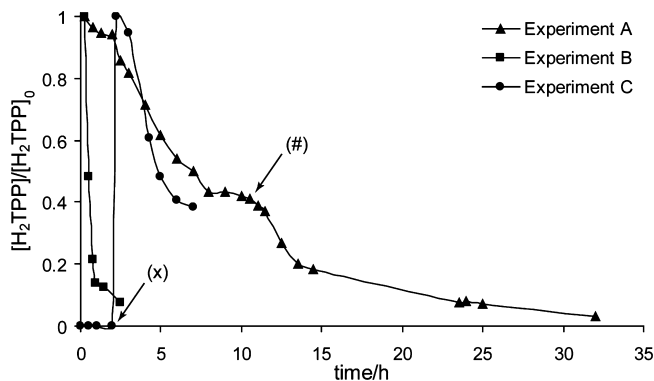


Figure 4. Metalation of H₂TPP with [Ru(DMF)₆](OTf)₃ (**1**) under conditions given in Expts. A, B, and C (see text); arrows indicate addition of water (#) or H₂TPP (x).

of H₂TPP was calculated and plotted as a function of time (Figure 4.) The trace is not that of a simple kinetic profile. During the first 2 h, Ru insertion is slow, possibly involving an induction period after which the metalation accelerated, but leveled off at 8 h; CO₂ production was evident throughout the 8 h. From 8 to 10 h, both metalation and Ru reduction slowed down considerably, as indicated by UV-vis analysis and the lack of BaCO₃ formation, respectively, although almost half of the initial free-base was still present and there was no sign of “over-reduction” of Ru to the metal. On addition of 10 μL (0.56 mmol) of deoxygenated H₂O, both metalation and CO₂ production resumed, establishing that unreacted Ru was present and, most importantly, that metalation is dependent on Ru^{III} reduction. After 32 h, Ru metal had deposited, while UV-vis analysis indicated ~97% conversion of H₂TPP, and after workup the isolated yield of Ru(TPP)(CO)(H₂O) was 96%. The total collected BaCO₃ was equivalent to 0.124 mmol of e⁻ (eq 1b), more than required to reduce the Ru^{III} to Ru^{II} (0.097 mmol). Fixation of CO₂ as BaCO₃ is not quantitative because some absorbed CO₂ may be present as bicarbonate that is not precipitated by Ba²⁺.⁴⁸ Any “lost” CO₂ and the excess 0.027 mmol of e⁻ presumably account for the observed Ru over-reduction, but measurement of the amount of Ru metal on the vessel walls was impractical.

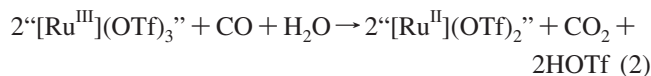
In Expt. B (again using 0.097 mmol Ru^{III}), 200 μL (11.1 mmol) of deoxygenated H₂O was added prior to the addition of **1**. The reaction now proceeded without an induction period and was complete in 2.5 h (Figure 4), accompanied by production of CO₂ and Ru metal; the H₂TPP conversion of ~90% realized a yield of only ~70% of isolated Ru(TPP)(CO)(H₂O), the fate of the ~20% H₂TPP being unknown. This experiment confirmed the role of adventitious water; in freshly opened DMF bottles, [H₂O] is ~10⁻³ mol L⁻¹, of the same order as concentrations of H₂TPP and **1**. The water in commercial DMF likely provides the driving force (or even limits the yields) for the Ru-metalation and provides a further example of the role of trace water in organic and organometallic transformations.⁸⁰

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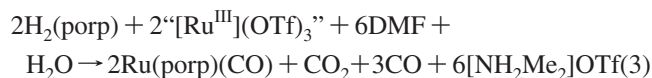
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In Expt. C, H₂TPP was added after [Ru(DMF)₆](OTf)₃ had been in refluxing DMF for 2 h (Figure 4). During this time, formation of BaCO₃ showed reduction of Ru and, as anticipated, metalation was fast upon addition of H₂TPP. The induction period seen in Expt. A is indeed associated with the reduction of Ru^{III} to, most likely, a Ru^{II} species (eq 2),



which is then incorporated into the porphyrin ring; no porphyrin species participate in the reduction process. Considering the affinity of Ru^{II} compounds for CO,^{19,81} and the continuous production of CO from thermal decomposition of DMF,⁸² this intermediate is probably a Ru^{II}–CO derivative. Of note, RuCl₃ in refluxing DMF yields several Ru carbonyl species, whose nature depends on the reaction conditions and workup procedure.⁸³ DMF decomposition can also be catalyzed by acids,⁸⁴ and so complex **1**, Ru-porphyrin, or any other Lewis acid Ru-species, may accelerate the reaction. Indeed, Ru^{II}-porphyrins under appropriate conditions are active catalysts for decarbonylation of aldehydes⁸⁵ and DMF itself,⁸⁶ while reaction of **1** with 2-methylimidazole in refluxing MeOH generates [Ru(CO)(DMF)(2-MeIm)₄](OTf)₂ via decarbonylation of coordinated DMF.^{35a} Less clear is whether the CO of the Ru(porp)(CO) products is derived from an intermediate Ru^{II}-carbonyl species, or from a putative Ru^{II}(porp)(DMF)₂ intermediate; abstraction of an acetyl group from coordinated *N,N*-dimethylacetamide has been observed in a Rh-porphyrin system.⁸⁷ For each equivalent of CO produced, one equivalent of NHMe₂ is also formed (eq. 1a), and this may be responsible for neutralization of the acid resulting from the reduction of Ru^{III} and from metalation. The overall reaction can be summarized in the speculative, stoichiometric eq 3.



We are unaware of similar systematic studies on porphyrin metalation using Ru₃(CO)₁₂.

Worth noting is that metalation of a free-base porphyrin with hydrated RhCl₃ in refluxing DMF generates [Rh^{III}(porp)(NHMe₂)₂]Cl,⁸⁸ bonding of the amine fragment being preferred over CO for the higher oxidation state metal

(vs Ru^{II}); nonmetalation was noted when anhydrous RhCl₃ was used,⁸⁸ and the water almost certainly reduces (cf. eqs 1b and 2) substitution-inert Rh^{III} to a labile Rh^I intermediate.⁸⁹ Similarly, Cu^{II} metalation of porphyrins in water is accelerated by the presence of reducing agents that generate in situ Cu^I ions.⁹⁰ The reported synthesis of [Rh(TPP)-(NHMe₂)₂]Cl via metalation with [Rh(CO)₂Cl]₂ in refluxing DMF requires air, presumably for reoxidation of a putative Rh^I-porphyrin intermediate.⁹¹ Details of the Rh systems remain uncertain since substitution-inert metal ions become less inert through pronounced cis-effects seen in metalloporphyrins.^{87,92} The use of metal salts (usually chlorides) for metalation of porphyrins in refluxing DMF is well established,⁹³ and mechanistic aspects revealed in our studies with [Ru(DMF)₆](OTf)₃ are likely quite general.

Ru-Metalation of Schiff-Bases. Application of the [Ru(DMF)₆](OTf)₃ method for metalation of Schiff-bases revealed a key difference from the porphyrin systems in that CO-free, Ru^{III} complexes were isolated. Metalation of H₂^tBu₄Salen and H₂^tBu₄Salophen, as monitored by TLC, was complete in 3 h, the conversion of free-base being accompanied by the appearance of dark blue or dark green species, respectively. The complexes were isolated by chromatography (SiO₂, 10:1 CH₂Cl₂/EtOH), and characterized as [Ru(Schiff-base)(DMF)₂]OTf species by elemental analysis, UV–vis, IR, conductivity, and MS, but attempts at crystallization were unsuccessful.

The observed single ν_{CO} band at 1637/1638 cm⁻¹ (vs 1673 cm⁻¹ for free DMF) is consistent with the presence of trans-DMF ligands and is in accordance with data for other Ru^{III}-DMF complexes.⁹⁴ The tetradentate [N₂O₂] Schiff-base presumably occupies the equatorial plane, although there are examples where the Schiff-base ligand is nonplanar.^{44b} The ionic character of the triflate was demonstrated by conductivity data (in DMF), which are in the range for 1:1 electrolytes,⁹⁵ and by the IR data (ν_{SO₃} and ν_{CF₃} at 1267/1268 and 1031 cm⁻¹), which agree with literature values for ionic OTf⁻ rather than oxygen-coordinated triflate.⁹⁶ The UV–vis spectra of the two complexes, presented in Supporting Information, Figure S2, are similar to those of other Ru^{III}-compounds such as Ru(Salen)(PPh₃)Cl;^{27b} the visible region is dominated by a broad, ligand-to-metal charge-transfer band at 700–900 nm, which is shifted to ~500 nm in Ru^{II} derivatives.^{8f} (Of note, UV–vis spectra of Ru^{III}-porphyrins also show a characteristic, broad band in the 700–900 region^{1g}).

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Work-up of the Ru-complexes, at the stage when TLC analysis of the crude product mixtures showed complete consumption of free-base, gave only ~50% isolated yields. ¹H NMR analysis of the colorless fraction revealed, as well as DMF, the presence of *tert*-butylsalicylaldehyde as shown by comparison of its NMR spectrum with that of an authentic, commercial sample; hydrolysis of a Schiff-base to its constituent aldehyde and amine, which is susceptible to catalysis by transition metals, is well-known.^{80b,97} Thus, water plays a positive role in the metalation of porphyrins (previous Sections), and a negative role in the Schiff-base systems. Pure complexes were not obtained with the non-*tert*-butyl-substituted Schiff-bases, H₂(Salen), H₂Salophen, and H₂Naphthophen; MS data of crude product mixtures showed that metalation did occur but chromatography and crystallization procedures were unsuccessful.

Concluding Remarks

A new, convenient and efficient methodology for insertion of Ru into a range of free-base porphyrins is described using [Ru(DMF)₆](OTf)₃, which is made via a simple literature procedure. The in situ reduction of Ru^{III} to Ru^{II} in refluxing “wet” DMF under Ar, coupled with CO abstraction from

the solvent, gives Ru^{II}(porp)(CO) complexes in yields comparable to, or higher than, those obtained via the established method using thermal oxidative-decarbonylation of Ru₃(CO)₁₂. No Ru-chlorin impurity is detected when using the [Ru(DMF)₆](OTf)₃ method, thus eliminating a postmetalation benzoquinone oxidative step typically necessary when using the Ru₃(CO)₁₂ method. Limitations of this new method are associated with di-*ortho* substituted *meso*-tetraarylporphyrins, a porphyrin with an N-Me substituent, and porphyrins that are unstable toward refluxing DMF. Comparisons between apparently dissimilar metalation of porphyrins with Ru, Rh, and Cu species in DMF suggest that the underlying mechanisms in these systems are closely related. The methodology was also extended to metalation of tetradentate Schiff-bases to yield chloride-free Ru complexes of general formula [Ru^{III}(N₂O₂-Schiff base)(DMF)₂](OTf).

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Supporting Information Available: ORTEP diagram (Figure S1) and cif file for Ru(OEP)(CO)(THF); UV-vis spectra in DMF of [Ru(^tBu₄Salen)(DMF)₂](OTf) and [Ru(^tBu₄Salophen)(DMF)₂](OTf) (Figure S2). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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