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Thiol, Disulfide, and Trisulfide Complexes of Ru Porphyrins: Potential Models for Iron–Sulfur Bonds in Heme Proteins

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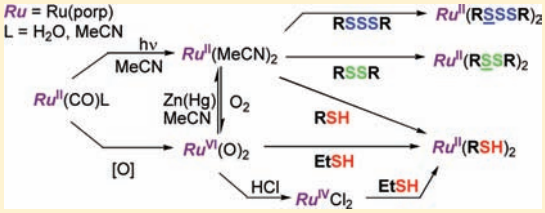
Supporting Information

ABSTRACT: Thirty-two Ru(porp)L_2 complexes have been synthesized, where porp = the dianion of *meso*-tetramesitylporphyrin (TMP) or *meso*-tetrakis(4-methylphenyl)porphyrin (H_2T-*p*Me-*PP*), and L = a thiol, a sulfide, a disulfide, or a trisulfide. Species studied were with RSH [R = Me, Et, ^{n}Pr, ^{i}Pr, ^{t}Bu, Bn (benzyl), and Ph], RSR (R = Me, Bn), RSSR (R = Me, Et, ^{n}Pr, Bn) and MeSS^{t}Bu, and RSSSR (R = Me, Bn). All the species except two, which were the isolated Ru(T-*p*Me-*PP*)(^{t}BuSH)$_2$ and Ru(TMP)(MeSSMe)$_2$, were characterized in situ. The disulfide complex was characterized by X-ray analysis. ^{1}H NMR data for the coordinated thiols are the first reported within metalloporphyrin systems, and are especially informative because of the upfield shifts of the axial sulfur-containing ligands due to the porphyrin π-ring current effect, which is also present in the di- and trisulfide species. The disulfide in the solid state structure of Ru(TMP)(MeSSMe)$_2$ is η^1(end-on) coordinated, the first example of such bonding in a nontethered, acyclic dialkyl disulfide; ^{1}H–^{1}H EXSY NMR data in solution show that the species undergoes 1,2-S-metallotropic shifts. Stepwise formation of the bis(disulfide) complex from Ru(TMP)(MeCN)$_2$ in solution occurs with a cooperativity effect, resembling behavior of Fe^{II}–porphyrin systems where crystal field effects dominate, but ligand trans-effects are more likely in the Ru system. The η^1(end-on) coordination mode is also favored for the trisulfide ligand. Discussed also are the remarkable linear correlations that exist between the ring-current shielding shifts for the axial ligand C^1 protons of Ru(porp)(RS$_x$R)$_2$ and x (the number of S atoms). The Introduction briefly reviews literature on Ru- and Fe porphyrins (including heme proteins) with sulfur-containing ligands or substrates, and relationships between our findings and this literature are discussed throughout the paper.



1. INTRODUCTION

Heme proteins that contain S-donor molecules as ligands proximal to the heme moiety are involved in a plethora of biological reactions and processes, in which Fe–S interactions play catalytic and/or structural roles.[1] In these systems, the S-donor is usually a residual cysteine or methionine group from the protein chain, but the Fe(heme)–sulfur bond can also result from interaction with a S-containing substrate or exogenous ligand (see below). The reactions at the Fe-center often involve ligand activation and redox processes, which are frequently accompanied by spin-state transitions (e.g., in cytochromes P450) that may complicate the study of these systems;[2] such complications are encountered also in biomimetic Fe–porphyrin models.[3] In contrast, Ru–porphyrin species, regardless of the metal oxidation state, are generally low-spin, and are useful in modeling low-spin heme systems/intermediates. In addition to studies from our group,[4] reports from others[5−8] have provided a general coordination framework for interactions between S-donor ligands and Ru porphyrins (see Chart 1). Some of these Ru species have already assisted in the identification/characterization of naturally occurring interactions between S-containing proteins and the heme moiety (see below).

Our group was the first to report (in 1987) on well-defined, S-ligated Ru–porphyrin complexes, when studies on the O_2-oxidation of thioethers catalyzed by Ru porphyrins led to characterization of complexes with thioethers and S- and O-bonded sulfoxides as axial ligands (Chart 1, a–d).[4a−d] The complex Ru(OEP)(DMSO)$_2$ (OEP = dianion of β-octaethylporphyrin) was reported in 1975, but was uncharacterized, with even the elemental analysis being unsatisfactory.[9] Although our studies were primarily focused on mono- and dioxygenase-type catalytic activity, the Ru complexes are of value as models for methionine-ligated heme proteins, such as cytochrome *c* and bacterioferritin, where electronic and structural effects of the axial ligands on the metalloprotein properties continue to be of interest.[10,11] In cytochrome *c*, a protein involved in respiratory electron transport, the heme ligands are imidazole and thioether moieties from His-18 and Met-80, respectively (Chart 2, a). Under oxidative stress, the Met-80 may be oxidized to the sulfoxide (MetSO-80), which alters the structure and function of the protein, and it has been shown that the MetSO-80 is S-coordinated to the ferrous heme (Chart 2, b) but does not bind to the ferric heme.[10] The thioether and sulfoxide Ru–porphyrin complexes have been recognized as convenient models for the native and oxidatively damaged cytochrome c, respectively.[10] Further, bond lengths and angles

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Chart 1. Ruthenium Porphyrins With Sulfur Ligands

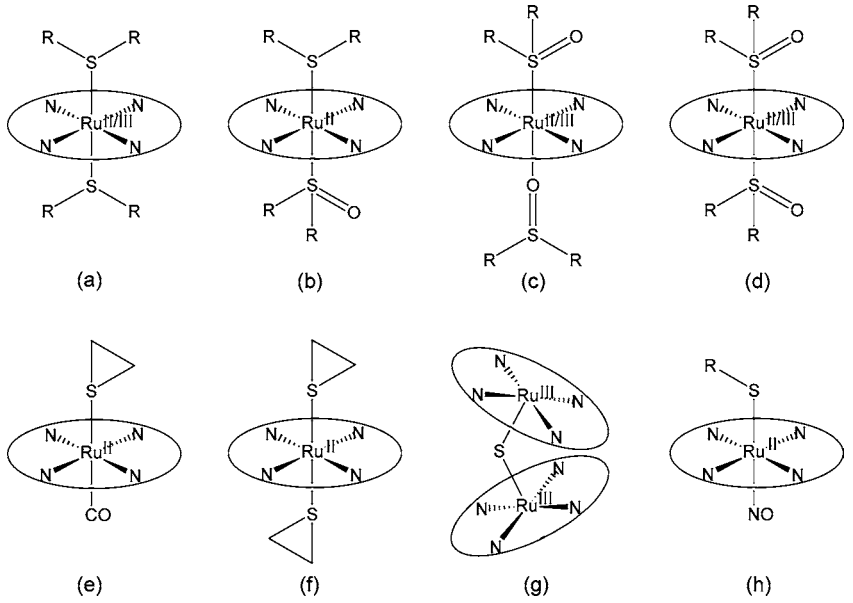
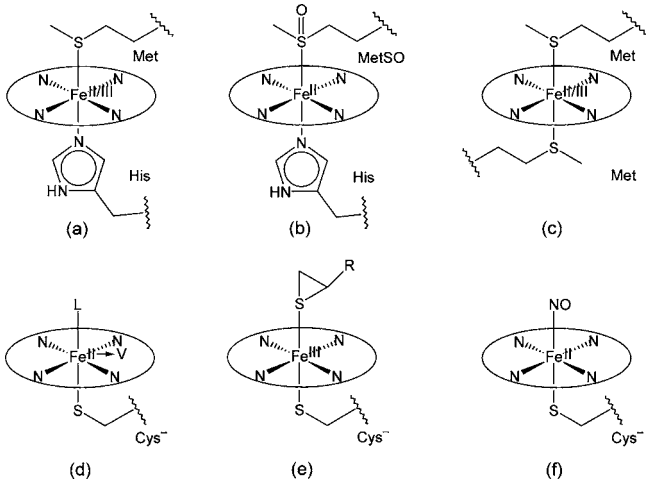


Chart 2. Some Iron Porphyrins With Sulfur Ligands (L = Various Ligands)



in the Ru^{II}– and Ru^{III}–bis(thioether) complexes are not significantly different,[4g] mimicking a functional feature of cytochrome *c*, where the reversible Fe^{III}/Fe^{II} redox process involves minimal structural change;[12] similar behavior has also been observed in Fe–porphyrin-based model systems.[12] Bacterioferritin, which has a heme moiety with axially coordinated methionine residues (Chart 2c),[13] is usually associated with mobile iron storage, but its physiological function has not been definitely established.[11b] The Fe-center is low-spin in both Fe^{II} and Fe^{III} oxidation states,[11b] a common feature of all bis(thioether) Ru–porphyrin complexes.[4a,b] Our group has also reported the water-soluble complex, $Na_4[Ru(porp)(S\text{-}DMSO)_2]$ (porp = *meso*-tetrakis(4-sulfonatophenyl)porphyrin) for use as a potential radiosensitizer,[4f] while the neutral TPP analogue has been reported by others in connection with catalytic oxidations.[14]

Episulfide (thiirane) complexes of Ru porphyrins (Chart 1, e) have provided a useful model for the "side-on" transition state of olefin epoxidation with oxo-metalloporphyrins and, ultimately, oxo-ferryl monooxygenases.[5] Measured binding constants of episulfides were larger than those of the corresponding epoxides and, although not noted in the original work,[5b] these results have significant implications in some drug design, where epoxide- and episulfide-substituted androgens have been tested as inhibitors of aromatase cytochromes P450 (Chart 2, d): the latter are ∼5-fold more effective likely due to the relative binding-affinity to the heme group (Chart 2, e).[15] The cysteinate-ligated heme proteins constitute the rate-limiting component of the enzymes in the biosynthesis of endogenous estrogens via androgen aromatization and, because of the physiological role of estrogen in hormone-dependent cancers, these enzymes are important medicinal targets for drug design and cancer treatments.[16] The bis(episulfide) complex (Chart 1, f) is a precursor to a Ru_2^{III} species (Chart 1, g) with bent geometry at the μ-S moiety, which contrasts with the linear geometry of the μ-oxo homologue.[8]

Thiolate-ligated Ru(nitrosyl) porphyrins (Chart 1, h) have been studied as models[6,7] of heme-thiolate proteins, specifically the nitric oxide synthases, which are cysteinate-ligated heme enzymes (Chart 2, f) responsible for the biosynthesis of NO.[17] One synthetic reaction of note is the net trans-addition of an organic thionitrite to a Ru(carbonyl) porphyrin (eq 1).[6a,c] Details on the model compounds and their relevance to biological systems have been reviewed.[6f] Protonation of the cysteinate ligand of cytochrome P450 to the cysteine-ligated form, at least in the ferrous state (Chart 3, a), is thought to give the inactive, so-called cytochrome P420;[18] attempts to generate a coordinated thiol via protonation of the Ru(porp)(NO)(SR) complexes were unsuccessful, the chemistry resulting in cleavage of the Ru–S bond.[6d]

$$\mathrm{Ru(porp)(CO) + RS(NO) \rightarrow Ru(porp)(NO)(SR) + CO} \quad (1)$$

Other biologically relevant S-containing compounds that interact with heme proteins, and for which (prior to our work) there were no Ru–porphyrin analogues, included MeSSMe, HS^-, and H_2S. Spectroscopic evidence supports coordination of MeSSMe to ferric cytochrome P450 (Chart 3, b),[19] and interaction of H_2S with cytochrome P450 yields a hydrosulfide complex (Chart 3, c),[19] whereas a mollusk H_2S-transport heme protein forms stable H_2S-adducts (Chart 3, d).[20] Examples of

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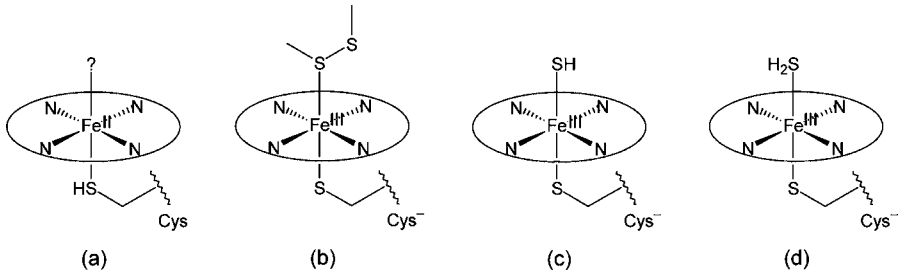
Chart 3. Heme Proteins With Coordinated Cysteine/Cysteinate



coordinated thiols and H_2S, including nonporphyrin chemistry, are relatively rare,[21] because attempted coordination of thiols (and H_2S) usually results in formation of the respective thiolato/hydrosulfido via deprotonation, or hydrido-thiolato species via oxidative addition, with the thiol- or H_2S-adduct usually been considered as an intermediate.[21]

The studies reported in this paper stemmed initially from interest in O_2-oxidation of thiols catalyzed by Ru−porphyrin complexes as a model for oxygenase systems, but as the research progressed, the interest expanded and became increasingly coupled to mimicking biological sulfur-containing systems. We found that thiols coordinate to Ru porphyrins to generate Ru(porp)$(RSH)_2$ products that could prove useful as biological models. During our thiol studies, disulfides were sometimes generated and these were also found to coordinate as such, rather than undergoing the more common oxidative addition reactions exemplified by eqs 2 and 3, processes that are not well-understood.[22] The studies were also extended to

$$\begin{aligned} M^{(n)} + RSSR &\rightarrow [M(\eta^1 - RSSR)] \\ &\rightarrow [M(\eta^2 - RSSR)] \\ &\rightarrow M^{(n+2)}(SR)_2 \end{aligned} \quad (2)$$

$$\begin{aligned} 2M^{(n)} + RSSR &\rightarrow \{[M(\eta^1 - RSSR)]+M\} \\ &\rightarrow [M_2(\mu - RSSR)] \\ &\rightarrow 2M^{(n+1)}(SR) \end{aligned} \quad (3)$$

include trisulfides. Although trisulfide-ligated heme proteins are currently unknown, trisulfides can show high anticarcinogenic and antiproliferatory activity, and modulation of cytochrome P450 has been implicated in such activity; see section 3.4.

2. EXPERIMENTAL SECTION

2.1. General. CH_3SH (CP, ≥99.5%) and anhydrous H_2S (technical purity, ≥ 99%) were used as received from Matheson Gas Co. All other thiols, sulfides, disulfides (except MeSS^tBu) and trisulfides were reagent grade and used as purchased from Aldrich Chemical Co. MeSS^tBu was prepared from the reaction between MeSSMe and ^{t}BuSH using a literature procedure;[24] the ^{1}H NMR spectra and GC analyses of the crude, isolated product (nondistilled) indicated that it was a mixture of MeSS^tBu (85%) and ^{t}BuSS^tBu (15%), which was used as such. All reactions and manipulations were carried out under anaerobic conditions, unless stated otherwise. Ar (Praxair, 99.996%) was percolated through an active Ridox column (Fisher Scientific). Benzene was treated with Na/benzoquinone, distilled under N_2, and used immediately. All solvents, including C_6D_6 purchased from Cambridge Isotope Laboratories, Inc., and liquid reagents were deoxygenated by purging with Ar. All general solvents and reagents were reagent grade and were used as supplied by Aldrich or Fisher Scientific. Suba-seal and rubber septa were thoroughly washed with CH_2Cl_2 and dried in an oven at 40 °C prior to use.

Elemental analysis was performed on a Carlo Erba EA 1108 analyzer. All ^{1}H NMR spectra were measured in C_6D_6 at room temperature (~295 K) on Bruker AV300 or AV400 spectrometers (300.13 and 400.13 MHz, respectively), and referenced to residual solvent protons of TMS-free C_6D_6 (δ 7.15); s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet (J values are given in Hz). MS data were collected on a Bruker Biflex matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) spectrometer. IR spectra (KBr) were recorded on a Nicolet 4700 FT-IR spectrometer. GC analysis of EtSSEt was done on a Hewlett-Packard 5890A instrument equipped with an H_2/air FID, and an HP 3392A integrator. The Praxair gases [air (breathing grade), H_2 (extra dry), and He (high ultrapure)] were purified with an activated charcoal trap (Supelco), while the He carrier gas was further purified using a high capacity gas purifier (Supelco). A semipolar high-resolution DB-17 GC column from J&W Scientific (30 m × 0.32 mm with film thickness 0.25 μm) was used, as well as a Chromosorb W-HP precolumn for retention of nonvolatile materials.

Figures and Tables deposited in the Supporting Information (SI) are labeled, respectively, Figures S1, S2, S3, S4, and Tables S1, S2.

2.2. Ru−Porphyrin Precursors. Ru(TMP)(CO)(H_2O),[25] Ru(T-*p*Me-*PP*)(CO)L (L = H_2O, MeCN),[26] Ru(TMP)$(O)_2$,[27] and Ru(TMP)Cl_2[28] were prepared using the reported methods (TMP = dianion of *meso*-tetramesitylporphyrin or *meso*-tetrakis(2,4,6-trimethylphenyl)porphyrin; T-*p*Me-*PP* = dianion of *meso*-tetrakis(4-methylphenyl)porphyrin). Air-sensitive Ru(TMP)$(MeCN)_2$ and Ru(T-*p*Me-*PP*)$(MeCN)_2$ samples were prepared via photolysis of the respective carbonyl precursor.[29] ^{1}H NMR data for Ru(TMP)$(MeCN)_2$ (in C_6D_6) and Ru(T-*p*Me-*PP*)$(MeCN)_2$ (in $CDCl_3$) agreed with literature values,[27b,30] and revealed purity of the compounds; additionally, IR spectra showed no carbonyl stretching vibration. All the chemistry involving *trans* bis-MeCN species was carried out in C_6D_6 at room temperature, and ^{1}H NMR data for the T-*p*Me-*PP* species in this solvent (not previously reported) are given below:

Ru(T-*p*Me-*PP*)$(MeCN)_2$: ^{1}H NMR δ 8.99 (s, 8H, β-pyrrole), 8.43 (AA′BB′, 8H, *o*-C_6H_4Me), 7.32 (AA′BB′, 8H, *m*-C_6H_4Me), 2.39 (s, 12H, *p*-CH_3), −2.14 (s, 6H, CH_3CN).

2.3. Ru(T-*p*Me-*PP*)(^{t}BuSH)$_2$. Ru(T-*p*Me-*PP*)$(MeCN)_2$, prepared from Ru(T-*p*Me-*PP*)(CO)(MeCN) (4.97 mg, 5.9×10^{-3} mmol) in a septum-sealed photolysis vial, was dissolved in C_6H_6 (2 mL), and then degassed ^{t}BuSH was added (0.50 mL, 4.44 mmol). The solution was shaken for 10 min, and then evaporation at room temperature over 24 h to dryness yielded Ru(T-*p*Me-*PP*)(^{t}BuSH)$_2$ quantitatively. Anal. Calcd for Ru(T-*p*Me-*PP*)(^{t}BuSH)$_2$, $C_{56}H_{56}N_4RuS_2$: C, 70.78; H, 5.94; N, 5.90. Found: C, 70.88; H, 5.93; N, 6.02. ^{1}H NMR: δ 8.80 (s, 8H, β-pyrrole), 8.22 (AA′BB′, 8H, *o*-C_6H_4Me), 7.32 (AA′BB′, 8H, *m*-C_6H_4Me), 2.40 (s, 12H, *p*-CH_3), −1.50 (s, 18H, $(CH_3)_3$CSH), −3.84 (s, 2H, ^{t}Bu*SH*).

2.4. Ru(TMP)(MeSSMe)$_2$. The above method, but using Ru(TMP)$(MeCN)_2$ prepared from Ru(TMP)(CO)(MeCN) (5.00 mg, 5.9×10^{-3} mmol), and degassed MeSSMe (0.10 mL, 1.11 mmol), yielded Ru(TMP)$(MeSSMe)_2$ quantitatively. Anal. Calcd for Ru(TMP)$(MeSSMe)_2$, $C_{60}H_{64}N_4RuS_2$: C, 67.32; H, 6.03; N, 5.23. Found: C, 67.22; H, 5.24; N, 4.98. ^{1}H NMR: δ 8.56 (s, 8H, β-pyrrole), 7.20 (m, 8H, *m*-$C_6H_2Me_3$), 2.46 (s, 12H, *p*-CH_3), 2.20 (s, 24H, *o*-CH_3), 0.13 (s, 6H, Ru-S-S(CH_3)), −1.65 (s, 6H, Ru-S-S(CH_3)-S).

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2.5. X-ray Analysis of Ru(TMP)(MeSSMe)$_2$. A brown, platelet crystal of Ru(TMP)(MeSSMe)$_2$·2C$_6$H$_6$ (0.30 mm × 0.25 mm × 0.10 mm) was grown from a mixture of Ru(TMP)(MeCN)$_2$ (~1 mg) and MeSSMe (~10 equiv) in C$_6$H$_6$ (0.50 mL) under Ar. X-ray analysis was conducted at 173 K using a Rigaku/ADSC CCD area detector with graphite monochromated Mo Kα radiation (λ = 0.71069 Å). The data were collected and processed using the d*TREK program,[31] and the structure was solved by direct methods[32] and expanded using Fourier techniques.[33] The final unit-cell parameters were based on 9101 reflections with $2\theta_{max}$ = 55.8°. The C$_6$H$_6$ molecules were disordered and were modeled using rigid groups in three orientations with relative populations of 0.5:0.25:0.25. All non-H atoms and those of the solvent molecules were refined anisotropically. The maximum and minimum residual densities on the final difference Fourier map corresponded to 0.715 and −0.517 e/Å^3, respectively. All calculations were performed using the teXsan[34] crystallographic software package. Full crystallographic data (CIF file) are given in the SI. Selected crystallographic data are listed in Table 1. The checkcif file reveals two B Alerts: the first results from the diffractometer being a prototype that had inadequate collision protection, which made it impossible to collect a complete data set on triclinic unit cells; the second alert is a consequence of H50 being part of a disordered benzene (over three sites), in which a minor fragment is adjacent to C28.

Table 1. Selected Crystallographic Data for Ru(TMP)(MeSSMe)$_2$·2C$_6$H$_6$

empirical formula	C$_{60}$H$_{64}$N$_4$S$_4$Ru·2C$_6$H$_6$	fw	1226.68
space group	P$\bar{1}$ (no. 2)	Z	1
a (Å)	10.5434(11)	D_{calc} g/cm^3	1.298
b (Å)	11.0635(19)	μ, cm^{-1}	4.28
c (Å)	14.3107(11	total reflns	13466
α (deg)	104.502(2)	unique reflns	6022
β (deg)	97.703(2)	$R(F)$ $(I \geq 2\sigma(I))^a$	0.039[c]
γ (deg)	99.046(4)	$wR2$ (F^2) (all data)[b]	0.105
V (Å^3)	1569.5(3)	GOF	1.09

[a] $R = \Sigma(||F_o| - |F_c||)/\Sigma|F_o|$. [b] $wR2 = [\Sigma (F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$. [c] 5264 observations.

2.6. In Situ, ^{1}H NMR-Scale Syntheses of Ru(porp)L$_2$ Species (L = RSH, RSR, RSSR′, RSSSR) from Ru(porp)(MeCN)$_2$ Complexes (porp = TMP or T-*p*Me-*PP*).

2.6.1. Gaseous and Liquid L. L = RSH with R = Me, Et, ^{n}Pr, ^{i}Pr, ^{t}Bu, Bn(benzyl), Ph; L = RSR with R = Me, Bn; L = RSSR with R = Me, Et, ^{n}Pr; and L = MeS^{t}Bu or MeSSSMe). In an Ar glovebox, 0.50 mL of a solution of Ru(porp)(MeCN)$_2$ in C$_6$D$_6$ (2.0 × 10^{-3} mol L^{-1}) was transferred to an NMR-tube capped with a septum. Outside the glovebox, degassed L (10 equiv per Ru, 10^{-3} mmol) was then added via a microsyringe. For the gaseous MeSH, the precursor solution was frozen at 0 °C, and the Ar headspace was replaced by MeSH (1 atm). In all cases, the exterior of the septum and the upper portion of the tube were wrapped with Parafilm to minimize O$_2$ diffusion. The tube was gently swirled, carefully avoiding contact between the solution and the septum (which absorbed the Ru complexes), and the ^{1}H NMR spectra were then recorded at 25 °C. The δ values are reported to the second decimal place, although analyses of different batches of Ru(porp)L$_2$ species indicated a ±0.005 ppm reproducibility. With in situ formation of all species, a ^{1}H signal for the dissociated C*H*$_3$CN (integrating to six protons) was seen at δ 0.59.

An NMR-scale reaction between H$_2$S and Ru(TMP)(MeCN)$_2$ in C$_6$D$_6$ followed the same procedure described for the reaction with MeSH, but with H$_2$S being used instead of MeSH.

Ru(TMP)(MeSH)$_2$: ^{1}H NMR: δ 8.47 (s, 8H, β-pyrrole), 2.44 (s, 12H, *p*-C*H*$_3$), 2.06 (s, 24H, *o*-C*H*$_3$), −2.22 (d, 6H, $^3J_{HH}$ = 7.59, C*H*$_3$SH), −4.04 (q, 2H, $^3J_{HH}$ = 7.59, MeS*H*). The signal for the mesityl *m*-protons (*m*-C$_6$*H*$_2$Me$_3$) was not observed and is assumed to be under the residual solvent signal at δ 7.15.

Ru(T-pMe-PP)(MeSH)$_2$: ^{1}H NMR: δ 8.75 (s, 8H, β-pyrrole), 8.13 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.29 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 2.41 (s, 12H, *p*-C*H*$_3$), −2.56 (d, 6H, $^3J_{HH}$ = 7.52, C*H*$_3$SH), −4.27 (q, 2H, $^3J_{HH}$ = 7.52, S*H*).

Ru(TMP)(EtSH)$_2$: ^{1}H NMR: δ 8.49 (s, 8H, β-pyrrole), 2.44 (s, 12H, *p*-C*H*$_3$), 2.09 (s, 24H, *o*-C*H*$_3$), −1.13 (t, 6H, $^3J_{HH}$ = 7.47, C*H*$_3$CH$_2$), −1.80 (m, 4H, $^3J_{HH}$ = 7.47, $^3J_{HH}$ = 7.35, C*H*$_2$SH), −3.93 (t, 2H, $^3J_{HH}$ = 7.35, S*H*). The *m*-C$_6$*H*$_2$Me$_3$ signal is assumed to be under the δ 7.15 solvent signal.

Ru(T-pMe-PP)(EtSH)$_2$: ^{1}H NMR: δ 8.80 (s, 8H, β-pyrrole), 8.18 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.29 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 2.39 (s, 12H, *p*-C*H*$_3$), −1.48 (t, 6H, $^3J_{HH}$ = 7.43, C*H*$_3$CH$_2$), −2.10 (m, 4H, $^3J_{HH}$ = 7.43, $^3J_{HH}$ = 7.23, C*H*$_2$SH), −4.10 (t, 2H, $^3J_{HH}$ = 7.23, S*H*).

Ru(TMP)(^{n}PrSH)$_2$: ^{1}H NMR: δ 8.49 (s, 8H, β-pyrrole), 2.44 (s, 12H, *p*-C*H*$_3$), 2.10 (s, 24H, *o*-C*H*$_3$), −0.60 (t, 6H, $^3J_{HH}$ = 7.19, C*H*$_3$CH$_2$), −0.70 to −0.81 (m, 4H, C*H*$_2$CH$_2$SH), −1.84 to −1.92 (m, 4H, C*H*$_2$SH), −3.93 (t, 2H, $^3J_{HH}$ = 8.37 Hz, S*H*). The *m*-C$_6$*H*$_2$Me$_3$ signal is under the δ 7.15 solvent signal.

Ru(T-pMe-PP)(^{n}PrSH)$_2$: ^{1}H NMR: δ 8.80 (s, 8H, β-pyrrole), 8.19 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.29 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 2.39 (s, 12H, *p*-C*H*$_3$), −0.66 (t, 6H, $^3J_{HH}$ = 7.29, C*H*$_3$CH$_2$), −1.23 to −1.31 (m, 4H, C*H*$_2$CH$_2$SH), −2.09 to −2.16 (m, 4H, C*H*$_2$SH), −4.09 (t, 2H, $^3J_{HH}$ = 7.11, S*H*).

Ru(TMP)(^{i}PrSH)$_2$: ^{1}H NMR: δ 8.47 (s, 8H, β-pyrrole), 2.44 (s, 12H, *p*-C*H*$_3$), 2.11 (s, 24H, *o*-C*H*$_3$), −1.19 (d, 12H, $^3J_{HH}$ = 6.69, (C*H*$_3$)$_2$CH), −1.56 (m, 2H, $^3J_{HH}$ = 6.69, $^3J_{HH}$ = 1.86, C*H*SH), −3.82 (d, 2H, $^3J_{HH}$ = 1.86, S*H*). The *m*-C$_6$*H*$_2$Me$_3$ signal is assumed to be under the δ 7.15 solvent signal.

Ru(T-pMe-PP)(^{i}PrSH)$_2$: ^{1}H NMR: δ 8.78 (s, 8H, β-pyrrole), 8.18 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.31 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 2.39 (s, 12H, *p*-C*H*$_3$), −1.43 (d, 12H, $^3J_{HH}$ = 6.60, (C*H*$_3$)$_2$CH), −1.69 (m, 2H, $^3J_{HH}$ = 6.60, $^3J_{HH}$ = 2.52, (CH$_3$)$_2$C*H*), −4.02 (d, 2H, $^3J_{HH}$ = 2.52, S*H*).

Ru(TMP)(^{t}BuSH)$_2$: ^{1}H NMR: δ 8.51 (s, 8H, β-pyrrole), 7.17 (s, 8H, *m*-C$_6$*H*$_2$Me$_3$), 2.44 (s, 12H, *p*-C*H*$_3$), 2.19 (s, 24H, *o*-C*H*$_3$), −1.29 (s, 18H, (C*H*$_3$)$_3$C), −3.70 (s, 2H, S*H*).

Ru(T-pMe-PP)(^{t}BuSH)$_2$: ^{1}H NMR: δ 8.80 (s, 8H, β-pyrrole), 8.22 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.32 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 2.40 (s, 12H, *p*-C*H*$_3$), −1.50 (s, 18H, (C*H*$_3$)$_3$C), −3.84 (s, 2H, S*H*). These data are identical to those of the isolated Ru(T-*p*Me-*PP*)(^{t}BuSH)$_2$ species.

Ru(TMP)(BnSH)$_2$: ^{1}H NMR: δ 8.57 (s, 8H, β-pyrrole), 7.12 (s, 8H, *m*-C$_6$*H*$_2$Me$_3$), 6.46−6.40 (m, 2H, *p*-C$_6$*H*$_5$CH$_2$), 6.36−6.31 (m, 4H, *m*-C$_6$*H*$_5$CH$_2$), 5.43−5.40 (m, 4H, *o*-C$_6$*H*$_5$CH$_2$), 2.41 (s, 12H, *p*-C*H*$_3$), 2.07 (s, 24H, *o*-C*H*$_3$), −0.65 (d, 4H, $^3J_{HH}$ = 8.64, PhC*H*$_2$), −3.41 (t, 2H, $^3J_{HH}$ = 8.64, S*H*).

Ru(T-pMe-PP)(BnSH)$_2$: ^{1}H NMR: δ 8.83 (s, 8H, β-pyrrole), 8.15 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.27 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 6.44−6.38 (m, 2H, *p*-C$_6$*H*$_5$CH$_2$), 6.33−6.27 (m, 4H, *m*-C$_6$*H*$_5$CH$_2$), 5.17−5.13 (m, 4H, *o*-C$_6$*H*$_5$CH$_2$), 2.39 (s, 12H, *p*-C*H*$_3$), −0.94 (d, 4H, $^3J_{HH}$ = 7.66, PhC*H*$_2$), −3.74 (t, 2H, $^3J_{HH}$ = 7.66, S*H*).

Ru(TMP)(PhSH)$_2$: ^{1}H NMR: δ 8.50 (s, 8H, β-pyrrole), 6.21−6.16 (m, 2H, *p*-C$_6$*H*$_5$SH), 5.91−5.89 (m, 4H, *m*-C$_6$*H*$_5$SH), 4.13−4.09 (m, 4H, *o*-C$_6$*H*$_5$SH), 2.44 (s, 12H, *p*-C*H*$_3$), 1.96 (s, 24H, *o*-C*H*$_3$), −2.09 (s, 2H, S*H*). The *m*-C$_6$*H*$_2$Me$_3$ signal is assumed to be under the δ 7.15 solvent signal.

Ru(T-pMe-PP)(PhSH)$_2$: ^{1}H NMR: δ 8.71 (s, 8H, β-pyrrole), 8.09 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.34 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 6.45−6.39 (m, 2H, *p*-C$_6$*H*$_5$SH), 6.09−6.03 (m, 4H, *m*-C$_6$*H*$_5$SH), 3.85−3.81 (m, 4H, *o*-C$_6$*H*$_5$SH), 2.43 (s, 12H, *p*-C*H*$_3$), −2.50 (s, 2H, S*H*).

Ru(TMP)(MeSMe)$_2$: ^{1}H NMR: δ 8.43 (s, 8H, β-pyrrole), 2.44 (s, 12H, *p*-C*H*$_3$), 2.12 (s, 24H, *o*-C*H*$_3$), −2.03 (s, 12H, S(C*H*$_3$)$_2$). The *m*-C$_6$*H*$_2$Me$_3$ protons were not detected.

Ru(T-pMe-PP)(MeSMe)$_2$: ^{1}H NMR: δ 8.71 (s, 8H, β-pyrrole), 8.09 (AA′BB′, 8H, *o*-C$_6$*H*$_4$Me), 7.28 (AA′BB′, 8H, *m*-C$_6$*H*$_4$Me), 2.39 (s, 12H, *p*-C*H*$_3$), −2.23 (s, 12H, S(C*H*$_3$)$_2$).

Ru(TMP)(BnSBn)$_2$: ^{1}H NMR: δ 8.56 (s, 8H, β-pyrrole), 6.38−6.33 (m, 4H, S(CH$_2$-*p*-C$_6$*H*$_5$)$_2$), 6.25−6.21 (m, 8H, S(CH$_2$-*m*-C$_6$*H*$_5$)$_2$), 5.26−5.23 (m, 8H, S(CH$_2$-*o*-C$_6$*H*$_5$)$_2$), 2.41 (s, 12H, *p*-C*H*$_3$), 2.18 (s,

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24H, *o*-CH_3), −0.43 (s, 8H, S(CH_2Ph)$_2$). The mesityl *m*-protons were not detected.

Ru(T-pMe-PP)(BnSBn)$_2$: ^{1}H NMR: δ 8.81 (s, 8H, β-pyrrole), 8.15 (AA′BB′, 8H, *o*-C_6H_4Me), 7.25 (AA′BB′, 8H, *m*-C_6H_4Me), 6.47−6.42 (m, 4H, S(CH_2-*p*-C_6H_5)$_2$), 6.36−6.30 (m, 8H, S(CH_2-*m*-C_6H_5)$_2$), 5.14−5.11 (m, 8H, S(CH_2-*o*-C_6H_5)$_2$), 2.37 (s, 12H, *p*-CH_3), −0.59 (s, 8H, S(CH_2Ph)$_2$).

Ru(TMP)(MeSSMe)$_2$: ^{1}H NMR: δ 8.56 (s, 8H, β-pyrrole), 7.20 (s, 8H, *m*-$C_6H_2Me_3$), 2.46 (s, 12H, *p*-CH_3), 2.20 (s, 24H, *o*-CH_3), 0.13 (s, 6H, MeSSCH_3), −1.65 (s, 6H, CH_3SSMe). These data are identical to those of the isolated Ru(TMP)(MeSSMe)$_2$.

Ru(T-pMe-PP)(MeSSMe)$_2$: ^{1}H NMR: δ 8.85 (s, 8H, β-pyrrole), 8.23 (AA′BB′, 8H, *o*-C_6H_4Me), 7.32 (AA′BB′, 8H, *m*-C_6H_4Me), 2.40 (s, 12H, *p*-CH_3), −0.12 (s, 6H, MeSSCH_3), −1.92 (s, 6H, CH_3SSMe).

Ru(TMP)(EtSSEt)$_2$: ^{1}H NMR: δ 8.54 (s, 8H, β-pyrrole), 7.22 (s, 8H, *m*-$C_6H_2Me_3$), 2.46 (s, 12H, *p*-CH_3), 2.23 (s, 24H, *o*-CH_3), 0.62 (q, 4H, $^3J_{HH}$ = 7.28, EtSSCH_2), −0.26 (t, 6H, $^3J_{HH}$ = 7.28, EtSSCH_2CH_3), −0.75 (t, 6H, $^3J_{HH}$ = 7.26, CH_3CH_2SSEt), −1.67 (q, 6H, $^3J_{HH}$ = 7.26, CH_3CH_2SSEt).

Ru(T-pMe-PP)(EtSSEt)$_2$: ^{1}H NMR: δ 8.85 (s, 8H, β-pyrrole), 8.26 (AA′BB′, 8H, *o*-C_6H_4Me), 7.37 (AA′BB′, 8H, *m*-C_6H_4Me), 2.40 (s, 12H, CH_3), 0.43 (q, 4H, $^3J_{HH}$ = 7.17, EtSSCH_2CH_3), −0.31 (t, 6H, $^3J_{HH}$ = 7.17, EtSSCH_2CH_3), −1.03 (t, 6H, $^3J_{HH}$ = 7.23, CH_3CH_2SSEt), −1.80 (q, 4H, $^3J_{HH}$ = 7.23, CH_3CH_2SSEt).

Ru(TMP)(^{n}PrSS^{n}Pr)$_2$: ^{1}H NMR: δ 8.53 (s, 8H, β-pyrrole), 7.22 (s, 8H, *m*-$C_6H_2Me_3$), 2.46 (s, 12H, *p*-CH_3), 2.25 (s, 24H, *o*-CH_3), 0.68 (t, 4H, $^3J_{HH}$ = 7.28, ^{n}PrSSCH_2CH_2), 0.20−0.08 (m, 4H, ^{n}PrSSCH_2CH_2), 0.00 (t, 6H, $^3J_{HH}$ = 6.59, ^{n}PrSS$CH_2CH_2CH_3$), −0.25 to −0.40 (m, 10H, CH_2CH_2SS^{n}Pr and $CH_3CH_2CH_2$SS^{n}Pr), −1.71 (t, 4H, $^3J_{HH}$ = 6.42 Hz, $CH_3CH_2CH_2$SS^{n}Pr). A ^{1}H−^{1}H COSY NMR spectrum (Figure S1) was used to confirm the assignments for the ^{n}PrSS^{n}Pr moieties.

Ru(T-pMe-PP)(^{n}PrSS^{n}Pr)$_2$: ^{1}H NMR: δ 8.86 (s, 8H, β-pyrrole), 8.28 (AA′BB′, 8H, *o*-C_6H_4Me), 7.34 (AA′BB′, 8H, *m*-C_6H_4Me), 2.40 (s, 12H, CH_3), 0.49−0.43 (m, 4H, ^{n}PrSSCH_2), 0.08−0.02 (m, 10H, ^{n}PrSSCH_2CH_2 and ^{n}PrSS$CH_2CH_2CH_3$), −0.35 (t, 6H, $^3J_{HH}$ = 6.92, $CH_3CH_2CH_2$SS^{n}Pr), −0.65 to −0.78 (m, 4H, CH_2CH_2SS^{n}Pr), −1.77 (t, 4H, $^3J_{HH}$ = 7.55, CH_2SS^{n}Pr). A ^{1}H−^{1}H COSY NMR spectrum (Figure S2) was again used to confirm assignments for the disulfide moieties.

Ru(TMP)(MeSS^{t}Bu)$_2$: ^{1}H NMR: δ 8.53 (s, 8H, β-pyrrole), 7.21 (s, 8H, *m*-$C_6H_2Me_3$), 2.46 (s, 12H, *p*-CH_3), 2.26 (s, 24H, *o*-CH_3), −0.17 (s, 18H, MeSSC(CH_3)$_3$), −1.52 (s, 6H, CH_3SS^{t}Bu).

Ru(T-pMe-PP)(MeSS^{t}Bu)$_2$: ^{1}H NMR: δ 8.83 (s, 8H, β-pyrrole), 8.26 (AA′BB′, 8H, *o*-C_6H_4Me), 7.33 (AA′BB′, 8H, *m*-C_6H_4Me), 2.41 (s, 12H, *p*-CH_3), −0.24 (s, 18H, SSC(CH_3)$_3$), −1.77 (s, 6H, CH_3SS^{t}Bu).

Ru(TMP)(MeSSSMe)$_2$: ^{1}H NMR: δ 8.55 (s, 8H, β-pyrrole), 7.17 (s, 8H, *m*-$C_6H_2Me_3$), 2.44 (s, 12H, *p*-CH_3), 2.16 (s, 24H, *o*-CH_3), 0.78 (s, 6H, CH_3SSSCH_3), −1.45 (s, 6H, CH_3SSSCH_3).

Ru(T-pMe-PP)(MeSSSMe)$_2$: ^{1}H NMR: δ 8.83 (s, 8H, β-pyrrole), 8.16 (AA′BB′, 8H, *o*-C_6H_4Me), 7.30 (AA′BB′, 8H, *m*-C_6H_4Me), 2.40 (s, 12H, *p*-CH_3), 0.74 (s, 6H, CH_3SSSCH_3), −1.72 (s, 6H, CH_3SSSCH_3).

2.6.2. Solid L (L = BnSSBn, BnSSSBn). In an Ar glovebox, 0.50 mL of a solution of Ru(porp)(MeCN)$_2$ in C_6D_6 (2.0×10^{-3} mol L^{-1}) was transferred to a NMR tube containing L (10 equiv per Ru, 10^{-3} mmol). The tube was sealed with a septum, removed from the glovebox, and again wrapped with Parafilm.

Ru(TMP)(BnSSBn)$_2$: ^{1}H NMR: δ 8.62 (s, 8H, β-pyrrole), 6.77−6.68 (m, 6H, BnSSCH_2-*m*,*p*-C_6H_5), 6.50−6.35 (m, 6H, *m*,*p*-C_6H_5-CH_2SSBn), 5.90−5.85 (m, 4H, BnSSCH_2-*o*-C_6H_5), 5.75−5.71 (m, 4H, *o*-C_6H_5-CH_2SSBn), 2.43 (s, 12H, *p*-CH_3), 2.18 (s, 24H, *o*-CH_3), 1.25 (s, 4H, BnSSCH_2Ph), −0.49 (s, 4H, PhCH_2SSBn). The *m*-$C_6H_2Me_3$ protons were not detected.

Ru(T-pMe-PP)(BnSSBn)$_2$: ^{1}H NMR: δ 8.88 (s, 8H, β-pyrrole), 8.20 (AA′BB′, 8H, *o*-C_6H_4Me), 7.29 (AA′BB′, 8H, *m*-C_6H_4Me), 6.90−6.79 (m, 6H, BnSSCH_2-*m*,*p*-C_6H_5), 6.44−6.39 (m, 2H, *p*-C_6H_5-CH_2SSBn), 6.29−6.23 (m, 4H, *m*-C_6H_5-CH_2SSBn), 5.88−5.80 (m, 4H, BnSSCH_2-*o*-C_6H_5), 5.48−5.42 (m, 6H, *o*-C_6H_5-CH_2SSBn), 2.40 (s, 12H, *p*-CH_3), 1.08 (s, 4H, BnSSCH_2Ph), −0.72 (s, 4H, PhCH_2SSBn).

Ru(TMP)(BnSSSBn)$_2$: ^{1}H NMR: δ 8.63 (s, 8H, β-pyrrole), 7.17 (s, 8H, *m*-$C_6H_2Me_3$), 6.77−6.71 (m, 6H, BnSSSCH_2-*m*,*p*-C_6H_5), 6.42−6.37 (m, 6H, *m*,*p*-C_6H_5-CH_2SSSBn), 6.31−6.26 (m, 4H, BnSSSCH_2-*o*-C_6H_5), 5.72−5.68 (m, 4H, *o*-C_6H_5-CH_2SSSBn), 2.43 (s, 12H, *p*-CH_3), 2.27 (s, 24H, *o*-CH_3), 2.00 (s, 4H, BnSSSCH_2Ph), −0.37 (s, 4H, PhCH_2SSSBn).

Ru(T-pMe-PP)(BnSSSBn)$_2$: ^{1}H NMR: δ 8.92 (s, 8H, β-pyrrole), 8.22 (AA′BB′, 8H, *o*-C_6H_4Me), 7.25 (AA′BB′, 8H, *m*-C_6H_4Me), 6.83−6.77 (m, 6H, BnSSSCH_2-*m*,*p*-C_6H_5), 6.47−6.40 (m, 2H, *p*-C_6H_5-CH_2SSSBn), 6.39−6.29 (m, 8H, *m*-C_6H_5-CH_2SSSBn and BnSSSCH_2-*o*-C_6H_5), 5.56−5.49 (m, 6H, *o*-C_6H_5-CH_2SSSBn), 2.36 (s, 12H, *p*-CH_3), 2.31 (s, 4H, BnSSSCH_2Ph), −0.45 (s, 4H, PhCH_2SSSBn).

2.7. Equilibria Constants for the Ru(TMP)(MeCN)$_2$/MeSSMe System. Information on these was determined via a ^{1}H NMR titration method. A solution of Ru(TMP)(MeCN)$_2$ in C_6D_6 (2.65×10^{-3} mol L^{-1}; 0.45 mL) under Ar in a sealed NMR tube was titrated with aliquots (2.5−5.0 μL) of an anaerobic solution of MeSSMe in C_6D_6 (9.90×10^{-2} mol L^{-1}). After each addition, the mixture was shaken and the tube placed in the NMR probe for about 15 min prior to data acquisition. The tube was removed from the probe only for addition of MeSSMe in order to avoid temperature fluctuation; the probe and the disulfide solution were kept at 25.0 ± 0.1 °C. The dilution effect of the addition of the MeSSMe solution on the concentrations of Ru and MeSSMe was taken into account in the calculations.

3. RESULTS AND DISCUSSION

3.1. Coordination of Thiols, Sulfides, Disulfides, and Trisulfides. Bis-thiol, -sulfide, -disulfide, and -trisulfide Ru−porphyrin complexes were prepared by using Ru(porp)(MeCN)$_2$ and an excess of the sulfur-containing compound in benzene under anaerobic conditions. The relatively labile, diamagnetic MeCN precursors, prepared thermally[30] or photolytically[29] from Ru(porp)(CO)(solvent) species, have been widely used in syntheses of Ru−porphyrin complexes.[4d,h,27,35] The thiol studies were initiated using Ru(TMP)(MeCN)$_2$ species, because the sterically hindered Ru(TMP) moiety shows unique reactivity toward small molecules compared to non-ortho-substituted Ru porphyrins[4h,27b,36] like the H_2T*P*P-based systems exemplified here by Ru(T-*p*Me-*P*P)(MeCN)$_2$. The H_2TMP-based complexes (e.g., vs those of H_2T-*o*,*o*′Cl_2-*P*P, the *meso*-tetrakis(2,6-dichlorophenyl)porphyrin), which have been studied extensively in both diamagnetic and paramagnetic species,[4c,d,h,27,28b,30,35b,36,37] are particularly instructive in that the ^{1}H NMR signal(s) of the *o*-Me group provide(s) an excellent probe for the axial symmetry of the system.[4h,27b,36]

All the reactions described here, which are mainly in situ on an NMR scale, are completed quantitatively in ∼10 min, and isolation of Ru(T-*p*Me-*P*P)(^{t}BuSH)$_2$ and Ru(TMP)(MeSSMe)$_2$ in quantitiative yield exemplifies the synthetic methodolgy. The products are characterized by ^{1}H NMR, elemental analyses (for the isolated complexes) and, in the case of the disulfide, by X-ray crystallography. The reactants and products are all diamagnetic, and since the axial ligands were strongly shielded by the porphyrin ring current, the resonances for the coordinated ligands could be readily assigned even in the presence of excess ligand. Such use of metalloporphyrins as NMR shift reagents is well established.[4b,38]

3.2. Bis-Thiol and Bis-Sulfide Complexes. The Ru(porp)(RSH)$_2$ complexes (R = alkyl or aryl) containing TMP reveal a single ^{1}H resonance for the *o*-Me substituent, while the T-*p*Me-*P*P species show an AA′BB′ spin pattern for the phenyl protons, data that are consistent with a horizontal, symmetry plane structure. NMR studies covering the range δ +100 to −200 showed the absence of other diamagnetic or paramagnetic

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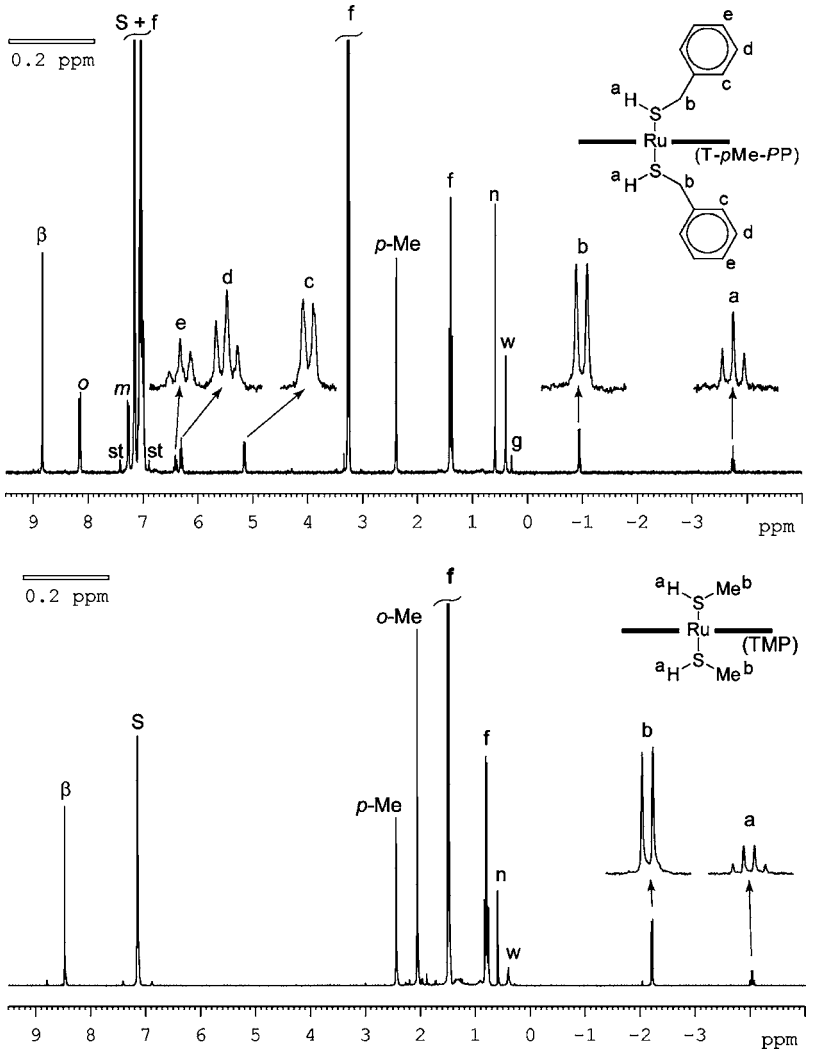

Figure 1. In situ ^{1}H NMR spectra (300 MHz) of Ru(T-*p*Me-*PP*)$(BnSH)_2$ (top) and Ru(TMP)$(MeSH)_2$ (bottom) with coordinated RSH signals expanded. Assignments: a, b, c, d, e, for coordinated RSH; *β* for *β*-pyrrole; f, free RSH; g, residual "grease"; *m* for *m*-C_6H_4; n, free MeCN; o for *o*-C_6H_4; S, residual C_6H_6; st, satellite signals (^{1}H−^{13}C coupling) of S; w, residual H_2O. *m*-C_6H_2 signal hidden under S signal.

species. The synthetic substitution reaction was characterized by the loss of the ^{1}H singlet of coordinated MeCN of the Ru(porp)$(MeCN)_2$ species (δ −1.33 and −2.14, respectively, for the TMP[27b,30] and T-*p*Me-*PP* species) and the appearance of a δ 0.59 signal for free MeCN (integrating to 6 protons).

Typical spectral changes for the *in situ* experiments are shown in Figure 1. Thiol proton assignments are based on the δ values, signal multiplicity and integration. The closer a proton is to the porphyrin plane, the more shielded it is, relative to the corresponding free ligand proton (Table 2); ^{1}H NMR data for the free thiols are given in Table S1. The two-proton, S*H* signal is the most upfield shifted because of its proximity to the porphyrin π-ring current. Of note, the Ru(T-*p*Me-*PP*) moiety is more effective than Ru(TMP) in shielding the axial ligand protons (Table 2); this porphyrin π-ring current effect has been studied more extensively using eight other porphyrins, and the findings[23] will be presented elsewhere. To the best of our knowledge, the NMR data in Table 2 are the first reported on thiol-bound metalloporphyrin complexes.

The ^{1}H NMR resonances of Ru(TMP)$(R_2S)_2$ and Ru(T-*p*Me-*PP*)$(R_2S)_2$ (R = Me, Bn) are readily assigned; upfield shifts for the alkyl moieties of the coordinated sulfides are similar to those reported previously for Ru(OEP)$(MeSMe)_2$.[4e] These shift data will be considered again with those of analogous disulfide and trisulfide complexes (see section 3.4)

The Ru(TMP)$(EtSH)_2$ complex was also prepared from Ru^{VI}(TMP)$(O)_2$ or Ru^{IV}(TMP)Cl_2 as shown in eqs 4 and 5, where the thiol is a reducing agent and the ligand donor. The metal reduction is accompanied by stoichiometric formation of EtSSEt, which was quantitatively identified in both reactions by ^{1}H NMR and GC analyses. Water, another coproduct in reaction 4, was also observed by ^{1}H NMR spectroscopy, whereas the necessary HCl coproduct in reaction 5 was not detected, most likely because of fast exchange with excess thiol.

$$\text{Ru(TMP)(O)}_2 + 6\text{EtSH} \rightarrow \text{Ru(TMP)(EtSH)}_2 + 2\text{EtSSEt} + 2\text{H}_2\text{O} \quad (4)$$

$$\text{Ru(TMP)Cl}_2 + 4\text{EtSH} \rightarrow \text{Ru(TMP)(EtSH)}_2 + \text{EtSSEt} + 2\text{HCl} \quad (5)$$

Scheme 1 outlines synthetic routes for Ru(TMP)$(RSH)_2$ (the amalgam reduction of Ru(TMP)$(O)_2$ to Ru(TMP)-$(MeCN)_2$ was reported by Groves et al.[30]). The bis(MeCN) species provide the cleanest synthesis, since the other routes

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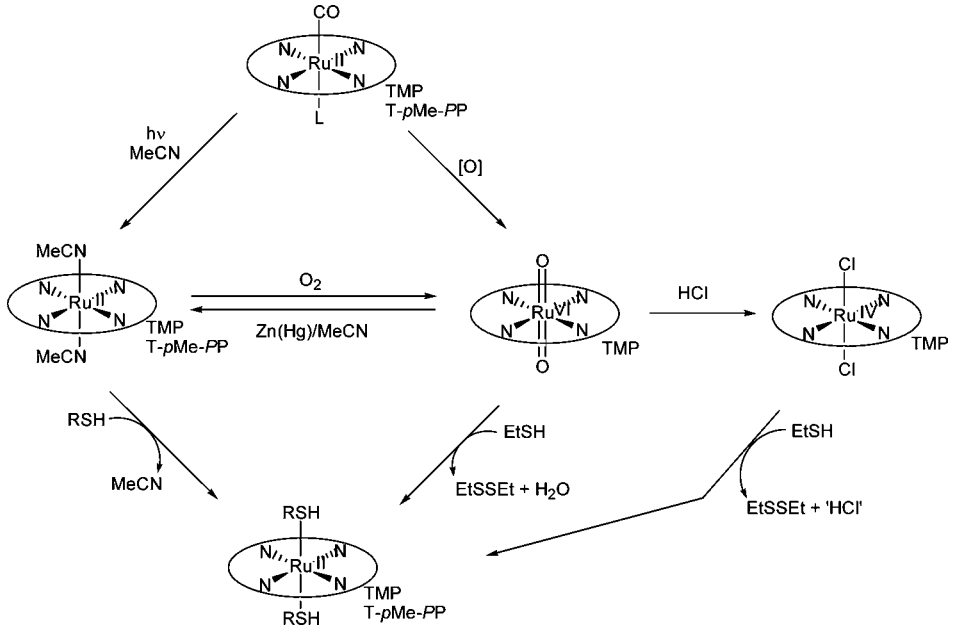
Table 2. Ring-current Effects in the Ru(porp)(RSH)$_2$ Species[a]

		$\Delta\delta_H = \delta_H$ (free thiol) − δ_H (coordinated thiol)						
Ru(porp)	RSH	*SH*	C^1*H*	C^2*H*	C^3*H*	*o*-*H*-Ph	*m*-*H*-Ph	*p*-*H*-Ph
Ru(TMP)	MeSH	4.84	3.71	–	–	–	–	–
	EtSH	4.99	3.87	2.07		–	–	–
	^{n}PrSH	4.95	3.95	2.05	1.31	–	–	–
	^{i}PrSH	5.15	4.29	2.23	–	–	–	–
	^{t}BuSH	5.31	–	2.49	–	–	–	–
	BnSH	4.80	3.90	–	–	1.62	0.69	0.60
	PhSH	5.09	–	–	–	2.86	0.96	0.67
Ru(T-*p*Me-*PP*)	MeSH	5.07	4.05	–	–	–	–	–
	EtSH	5.16	4.17	2.42	–	–	–	–
	^{n}PrSH	5.11	4.20	2.56	1.37	–	–	–
	^{i}PrSH	5.35	4.42	2.47	–	–	–	–
	^{t}BuSH	5.45	–	2.70	–	–	–	–
	BnSH	4.86	4.19	–	–	1.88	0.73	0.62
	PhSH	5.50	–	–	–	3.14	0.80	0.44

[a] δ values in ppm (C_6D_6); data for free thiols are given in Table S1.

Scheme 1. Synthetic Routes for Ru(TMP)(RSH)$_2$ Species



require separation of the bis(thiol) complexes from the RSSR coproducts. Further, reaction of Ru(TMP)(O)$_2$ with PhSH gives a mixture of Ru species, including the diamagnetic bis-thiolato Ru^{IV}(TMP)(PhS)$_2$,[23] suggesting some chemistry that is analogous to that of dioxo-Os^{VI} porphyrins, where reactions with arylthiols yield stable bis-arylthiolato Os^{IV} complexes.[39] Some details on the reactivity of Ru(TMP)(O)$_2$ toward thiols and on catalytic O_2-oxidation of the Ru(porp)(RSH)$_2$ species have been presented.[23,40]

Reports reveal that reactions between Fe porphyrins and thiols under anaerobic conditions in toluene (or benzene) are more complex than for the Ru systems: for example, Fe^{III} porphyrin derivatives react with alkylthiols to yield Fe^{II} species with no S-containing ligands,[41] whereas arylthiols produce Fe^{III}(porp)(arylthiolato) complexes, but these decompose in solution to yield thiolate-free Fe(II) species and the respective disulfide.[41a,42a,b] Spectroscopic evidence indicates that the intermediate(admixed)-spin,[43] four-coordinate, 'bare' Fe^{II}(porp) compounds are unreactive toward excess thiol,[41b,c] whereas addition of CO generates low-spin Fe(porp)(CO)(RSH) species.[41b,c,44] Of note, an Fe^{III}(TPP)(PhS) sample, cocrystallized with PhSH, changes in a reversible process at ~4 K from high- to low-spin with formation of Fe^{III}(TPP)(PhS)-(PhSH).[41a] The findings imply that thiols are weak ligands that might coordinate to Fe^{II}(porp) if this species undergoes a thermal transition to a low-spin state.[41b,c]

Thiol(cysteine)-bound, low-spin six-coordinate Fe^{II}–heme species have been proposed as short-lived intermediates in two heme protein-mediated processes,[45] and, in work from Dawson's group, spectroscopic evidence (UV–vis, MCD) suggests that low-spin Fe^{II}(porp)(RSH)$_2$ species can be formed at an Fe^{II}–heme center of an H93G myoglobin mutant,[18] thought to be Fe^{II}(porp)(H_2O).[46] Our findings on the low-spin Ru–porphyrin systems tend to corroborate the notion that low-spin Fe porphyrins bind thiols more strongly than high-spin species, although a mixture of five- and six-coordinate

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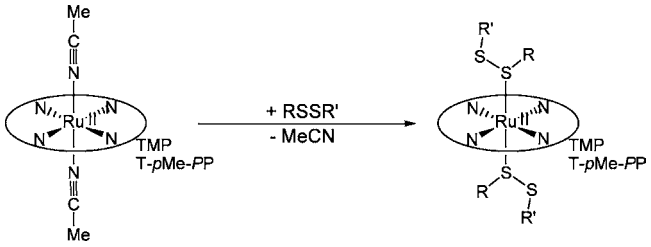
thiol(cysteine)-bound complexes in P420 (an inactive form of Fe^{II} cytochrome P450) has been suggested, and there is evidence for a high-spin, five-coordinate, Fe^{II} heme thiol adduct in a cytochrome *c* peroxidase mutant.[18] These are the only examples of thiol-ligated, high-spin, five-coordinate heme species. Whether the heme spin state controls neutral thiol coordination remains an open question. It is also possible that the high-spin, ferrous heme−thiol systems detected in Dawson's work[18] result from protein-induced constraints around the heme. To the best of our knowledge, no protein-free, five- or six-coordinate Fe^{II} porphyrin−thiol species have been reported. The Ru(porp)$(RSH)_2$ complexes may provide a convenient, room temperature entry for modeling thiol-ligated Fe porphyrin and heme protein systems.

3.3. Bis-Disulfide Complexes. Like the thiol complexes, the bis(disulfide) complexes are readily synthesized from the acetonitrile precursors (Scheme 2); they were generally made

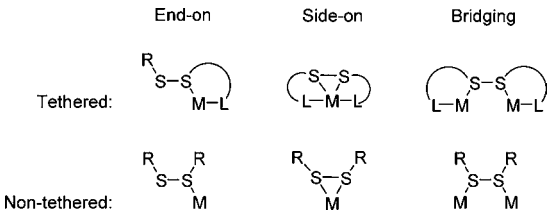
Scheme 2. Synthesis of Bis(disulfide) Species



in situ and characterized by ^1H NMR spectroscopy, but the species are isolable as shown for Ru(TMP)$(MeSSMe)_2$ that was more fully characterized using elemental analysis and an X-ray structure.

Disulfides are poor ligands,[47] and are usually tethered to a chelating ligand in order to assist their coordination via η^1-(end-on), η^2-(side-on), or a μ-fashion (Chart 4). Bridging

Chart 4. Binding Modes for Disulfide Ligands



disulfide complexes (tethered or not) comprise >60% of disulfide structures deposited in the Cambridge Crystallographic Database; the next most common coordination mode is tethered end-on, while side-on and nontethered end-on modes are rare. The side-on mode, often postulated as an intermediate in oxidative addition of disulfides to yield bis-thiolato complexes (see eq 2), has been established in $[NbCl_4(RSSR)_2]^+$ (R = Me, ^{i}Pr)[48a] and TiX_2L (L = an η^4-disulfide-bridged bis(phenolate) ligand).[48b] There are just three reported nontethered, end-on X-ray structures within the complexes $[Ag_2(Ph_2S_2)_4]^{2+}$,[49a] $W(CO)_5(SSCH_2CH{=}CHCH_2)$,[49b] and *S*-$Cu_2Br_4$-*S* (where *S* = a bonded S atom of a disulfide of a thiafulvalene system).[50]

The Ru(TMP)$(MeSSMe)_2$ structure (Figure 2) reveals η^1-binding for both disulfide ligands and is the first example with a nontethered, acyclic dialkyl disulfide. The geometry of the coordinated MeSSMe ligands is close to that of the free ligand[51a−d] (Table 3); even the S−S bond is only lengthed by ∼0.035 Å.

Data for the three other structurally characterized, nontethered, end-on disulfide complexes[49,50,51e−h] (Table 3) show the same general feature. The geometric parameters at the Ru center of the bis-disulfide are close to those of bis-sulfide and *S*-bound bis-sulfoxide complexes (Table 4), with the Ru−S bond length being in-between those of the sulfide and S-bonded sulfoxide complexes,[4b,g,14] where Ru→S π-back-bonding has been evoked. As shown in Chart 5 for the disulfide, some $d_{(Ru)}\rightarrow\sigma^*_{(S-S)}$ π-back-bonding is likely present via the Ru d_{xz} (or d_{yz}) orbital and the LUMO of MeSSMe,[52] and this would lead to a proportional weakening of the S−S bond, as observed (Table 3). Ferric cytochrome P450 is thought to bind MeSSMe via the same η^1-coordination (see Introduction, Chart 3, b).[19] The nonequivalence of the Me groups in the reported ^1H NMR spectrum of Rh(porp)(I)(MeSSMe) also implies an η^1-bonded disulfide.[53]

The ^1H NMR spectrum of Ru(TMP)$(MeSSMe)_2$ in C_6D_6 shows two upfield-shifted singlets (δ 0.13 and δ −1.65) for the Me groups of the η^1-MeSSMe moiety. The most shifted δ −1.65 signal (for the Me group closest to the porphyrin π-ring current) has a shift of 3.61 ppm, comparable with that of the CH_3SH signal of Ru(TMP)$(MeSH)_2$ (Table 2). Similar behavior is observed for other disulfides (Figure 3), and assignments for coordinated EtSSEt, BnSSBn, and MeSS^{t}Bu are straightforward (Table 5). For the ^{n}PrSS^{n}Pr species, some signals overlap, and assignments required $^1H-^1H$ COSY NMR experiments (see Figures S1, S2). As with the thiol systems, the Ru(T-*p*Me-*PP*) species reveal greater shielding effects than the corresponding Ru(TMP) species. The upfield NMR shifts of the MeSSMe and BnSSBn species will be discussed further in section 3.4 with those of the corresponding sulfide and trisulfide complexes.

Contrary to the aliphatic and aromatic thiols that all readily formed Ru(porp)$(RSH)_2$ (Scheme 1), the MeCN exchange with disulfide depended on substituents; for example, symmetric primary disulfides gave bis-η^1-$(RSSR)_2$ species (Table 5), whereas the tertiary one ^{t}BuSS^{t}Bu did not react. Secondary and aromatic symmetric disulfides, ^{i}PrSS^{i}Pr and PhSSPh, did react with Ru(porp)$(MeCN)_2$, but signals of the porphyrin and the coordinated disulfides were broadened. This behavior was not pursued, but it is reminiscent of that seen for Ru(OEP)$(PhSPh)_2$, where the axial sulfide becomes labile due to steric interactions between the phenyl groups and porphyrin ring, as established in a crystal structure analysis;[4b] the dynamic ligand exchange (seen at $\sim10^{-3}$ mol L^{-1} concentrations) was not seen with primary alkyl sulfides.[4b] That such steric effects are important in the disulfide ligand exchange was confirmed by a reaction with MeSS^{t}Bu, where coordination through the less sterically hindered sulfur was observed in both Ru(TMP) and Ru(T-*p*Me-*PP*) systems (Table 5). Coordination of ^{t}BuSS^{t}Bu to the sterically less demanding $[FeCp(CO)_2]^+$ has been reported.[54]

1,2-Metallotropic shifts (Scheme 3), which are established for $M(CO)_5(\eta^1$-RSSR) complexes (M = Cr, Mo, or W),[55] but are not seen in $[(Cp)Fe(CO)_2(\eta^1$-RSSR)$]BF_4$ species,[54] were demonstrated for Ru(TMP)$(MeSSMe)_2$ by a room temperature $^1H-^1H$ EXSY NMR experiment[56] (Figure 4). The off-diagonal peaks clearly demonstrate intramolecular rearrangement of C^1H_3S and $C^{1'}H_3S$ groups, and the participation of free

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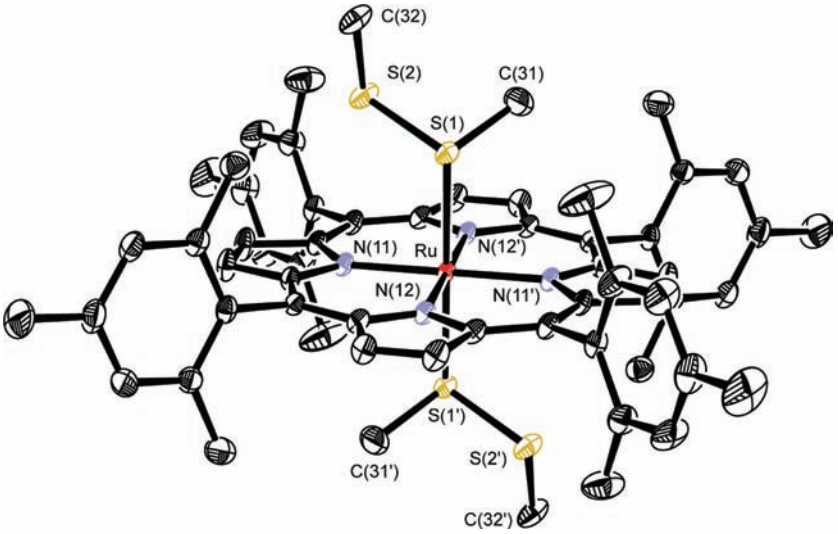
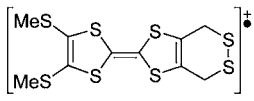


Figure 2. ORTEP diagram of Ru(TMP)(MeSSMe)$_2$, with thermal ellipsoids shown at the 50% probability level; the centrosymmetric structure has an inversion center at the Ru. Selected bond distances (Å) and bond angles (deg): Ru−S(1) 2.3504(7), Ru−N(11) 2.050(2), Ru−N(12) 2.050(2), S(1)−S(2) 2.0627(9), S(1)−C(31) 1.805(3), S(2)−C(32) 1.804(3), S(1)−Ru−N(11) 85.10(6), S(1)−Ru−N(11′) 94.90(6), S(1)−Ru−N(12) 91.73(6), S(1)−Ru−N(12′) 88.27(6), N(11)−Ru−N(12) 90.07(8), N(11)−Ru−N(12′) 89.93(8), Ru−S(1)−S(2) 107.76(3), Ru−S(1)−C(31) 108.57(11), S(2)−S(1)−C(31) 101.63(12), S(1)−S(2)−C(32) 100.45(11), Ru−S(1)−S(2)−C(32) 161.90(12), C(31)−S(1)−S(2)−C(32) −84.06(17).

Table 3. Selected Average Bond Lengths (Å) and Angles (deg) in End-on Disulfide Complexes, with Corresponding Data for the Free Ligand[a]

Disulfide		S-C	S-S	S-S-C	C-S-S-C	Ref.
MeSSMe	free	1.806(2)	2.022(3)	104.1(3)	83.9(9)	51a [b]
		1.816(3)	2.029(3)	103.2(2)	85(4)	51b [b]
		[1.784]	[2.066]	[107.0]	[76.1]	51c,d [c]
	bound	1.805(3)	2.0627(9)	101.04(11)	84.06(17)	t.w.[d]
PhSSPh	free	1.789(5)	2.023(1)	105.9(2)	85.0(2)[e]	51e
	bound	1.78(1)	2.080(3)	103.4(5)	67.6(3)[e]	49a
	free	1.815	2.056	98.5	61.9	51f [f]
	bound	1.82(2)	2.062(2)	98.1(4)	63.6(4)[e]	49b
	free	1.83(4)	2.011(8)	99.4(4)[e]	65.7(2)[e]	51g [g]
		1.795(6)	2.040(3)	98.2(2)[e]	65.5(3)[e]	51h [h]
	bound	1.81(2)	2.046(5)	97.9(8)	65.6(5)	50

[a]Estimated standard deviations in parentheses. [b]Gas-phase electron diffraction data. [c]Data (esd values unavailable) for a disordered MeSSMe moiety[51d] trapped in a complex crystal lattice.[51c] [d]t.w. = This work (Figure 2); S−S−C value is average of S(1)−S(2)−C(32) and S(2)−S(1)−C(31) values. [e]Calculated from CCDC CIF file. [f]Values are from ab initio geometry optimization data. [g]Counterion: I_3^-. [h]Counterion: $[CuCl_4]^{2-}$.

Table 4. Selected Average Bond Lengths (Å)[a] and Angles (deg)[a] in Ru(TMP)(MeSSMe)$_2$, Ru(OEP)("DecSMe)$_2$,[4b] Ru(OEP)(Ph$_2$S)$_2$,[4b] Ru(OEP)(Et$_2$SO)$_2$,[4g] and Ru(TPP)(DMSO)$_2$[14]

length or angle	Ru(TMP)(MeSSMe)$_2$	Ru(OEP)("DecSMe)$_2$[b]	Ru(OEP)(Ph$_2$S)$_2$	Ru(OEP)(Et$_2$SO)$_2$	Ru(TPP)(DMSO)$_2$
Ru−S	2.3504(6)	2.369(2)	2.371(1)	2.319(1)	2.3140(7)
Ru−N	2.052(4)	2.05(1)	2.049(3)	2.057(6)	2.045(4)
S−C	1.810(6)	1.811(8)	1.80(1)	1.78(2)	[c]
S−Ru−N (min.)	85.05(6)	86.9(1)	82.8(1)	88.2(1)	[c]
S−Ru−N (max)	94.95(6)	94.7(1)	97.2(1)	91.8(1)	[c]
S−Ru−S	180.0	178.27(3)	180.0	180.0	[c]
Ru−S−C	108.6(1)	109.0(4)	113.2(4)	112.4(6)	[c]
Ru−S−S	107.4(4)	–	–	–	–

[a]Standard deviations in parentheses. [b]Dec = decyl. [c]Disordered DMSO ligands.

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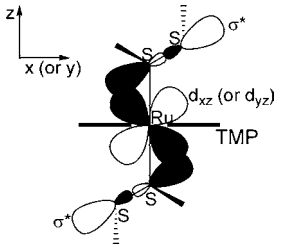
Chart 5. π-Back-bonding in the Disulfide Complex



ligand is ruled out by the absence of cross-peaks between coordinated and free disulfide.[55a] A side-on RSSR intermediate (Scheme 3) is usually invoked,[55a,c,d] implying a transient seven- or eight-coordinate Ru^{II} intermediate, depending on whether the 1,2-shift of each MeSSMe moiety occurs in a stepwise or concerted fashion, respectively, and both such species have been shown feasible within Ru^{II} (porp)−diphosphine complexes (Chart 6 a,b).[57] Of note, the distance between the Ru and the "dangling" sulfur in Ru(TMP)$(MeSSMe)_2$ is 3.57 Å, which is less than the sum of the van der Waals radii of S (1.80 Å)[58a] and Ru (2.30 Å),[58b] and suggests a weak interaction as in Chart 6 c; this could result from partial π-back-bonding to the $\sigma^*_{(S-S)}$ orbital of the disulfide (Scheme 4), which would polarize the S−S bond and lead to a partial increase in electron density on the "dangling" S atom, thereby contributing to the driving-force of the 1,2-shift. This perhaps implies that only a small reorganization energy is needed to sustain such an intramolecular rearrangement; indeed, for the $M(CO)_5(Me_3SiCH_2SSCH_2SiMe_3)$ systems (M = Cr, Mo, W), the $\Delta S^{\ddagger}$ value is only −9 to +8 J K^{-1} mol^{-1}.[55c]

An ^{1}H NMR titration of Ru(TMP)$(MeCN)_2$ with MeSSMe (Table S2) revealed the stepwise nature of disulfide binding via equilibria defined by K_1 and K_2 (eqs 6 and 7); the individual

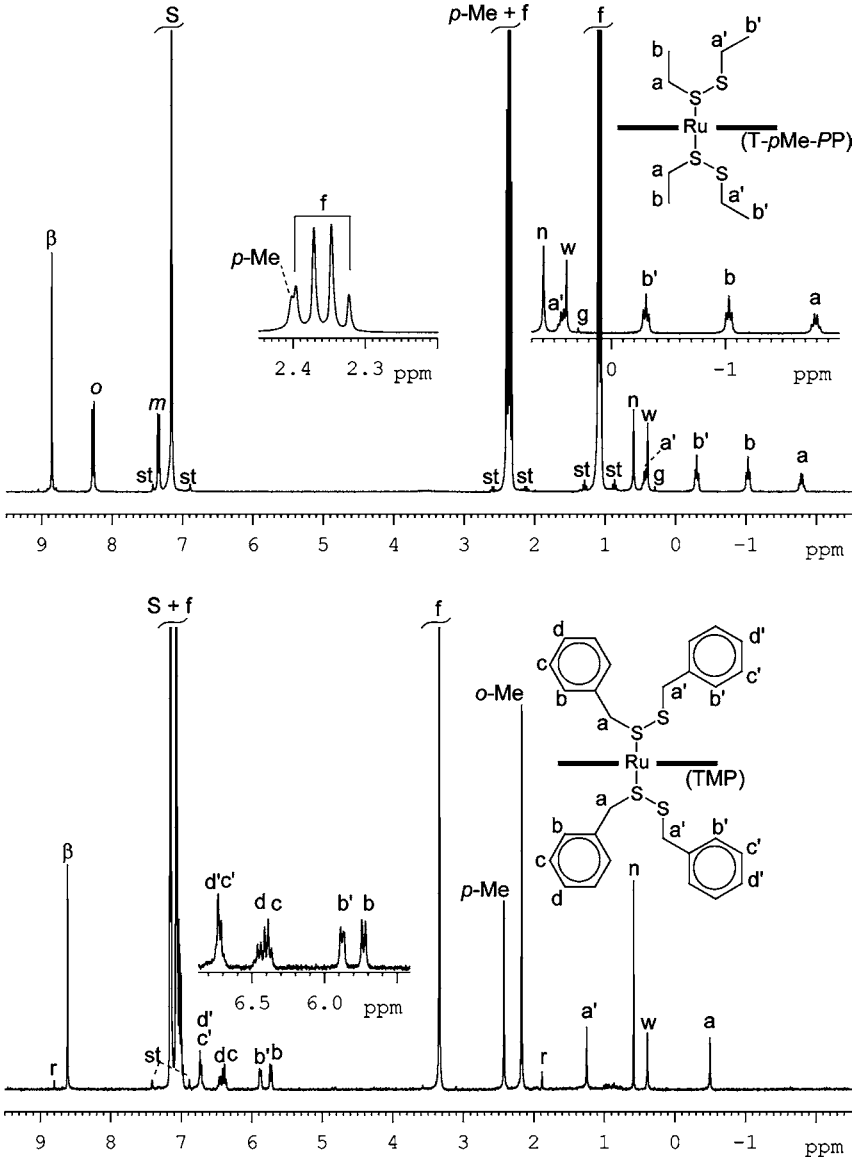


Figure 3. In situ ^{1}H NMR spectra (300 MHz, C_6D_6) of Ru(T-*p*Me-*PP*)$(EtSSEt)_2$ (top) and Ru(TMP)$(BnSSBn)_2$ (bottom); expanded regions have different scales. Assignments: a, a′, b, b′, c, c′, d, d′ for coordinated disulfide; β, β-pyrrole; f, free disulfide; g (see Figure 1 legend); *m*,*m*-C_6H_4; n, free MeCN; *o*, *o*-C_6H_4; S, residual C_6H_6; st, satellite (^{1}H−^{13}C coupling); r, Ru(TMP)(CO) impurity; w, residual H_2O. *m*-C_6H_2 signal hidden under S signal.

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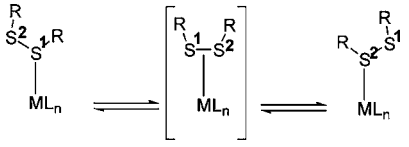
Table 5. Ring-Current Effects in Ru(porp)(RSSR′)$_2$ Species[a]

		$\Delta\delta_H = \delta_H$(free disulfide) − δ_H(coordinated disulfide)					
Ru(porp)	RSSR′	C^1H ($C'H$)	C^2H (C^2H)	C^3H (C^3H)	*o*-*H*-Ph (*o*-*H*-Ph′)	*m*-*H*-Ph (*m*-*H*-Ph′)	*p*-*H*-Ph (*p*-*H*-Ph′)
Ru(TMP)	MeSSMe	3.61	–	–	–	–	–
		(1.83)	–	–	–	–	–
	EtSSEt	4.02	1.82	–	–	–	–
		(2.61)	(0.45)	–	–	–	–
	^{n}PrSS^{n}Pr	4.11	1.87	1.11	–	–	–
		(1.72)	(1.40)	(0.78)	–	–	–
	BnSSBn	3.83	–	–	1.33	0.63	0.63
		(2.09)	–	–	(1.18)	(0.33)	(0.33)
	MeSS^{t}Bu	3.57	–	–	–	–	–
		(1.35)	–	–	–	–	–
Ru(T-*p*Me-*PP*)	MeSSMe	3.88	–	–	–	–	–
		(2.08)	–	–	–	–	–
	EtSSEt	4.15	2.10	–	–	–	–
		(2.66)	(0.64)	–	–	–	–
	^{n}PrSS^{n}Pr	4.17	2.26	1.13	–	–	–
		(1.94)	(1.49)	(0.73)	–	–	–
	BnSSBn	4.06	–	–	1.61	0.80	0.64
		(2.26)	–	–	(1.22)	(0.21)	(0.21)
	MeSS^{t}Bu	3.82	–	–	–	–	–
		(1.42)	–	–	–	–	–

[a] δ values in ppm (C_6D_6); data for free disulfides are given in Table S1.

Scheme 3. 1,2-Metallotropic Shifts in Disulfide Species



$$Ru(TMP)(MeCN)_2 + MeSSMe = Ru(TMP)(MeCN)(MeSSMe) + MeCN,\ K_1 \quad (6)$$

$$Ru(TMP)(MeCN)(MeSSMe) + MeSSMe = Ru(TMP)(MeSSMe)_2 + MeCN,\ K_2 \quad (7)$$

values are indeterminable since no free disulfide was detected at the NMR concentrations used until [MeSSMe$_{added}$] > [Ru$_{total}$]. The Ru(TMP)(MeCN)(MeSSMe) species was readily detected during the titration (Figures 5, 6, and Figures S3, S4.), since the axial nonsymmetry results in two singlets for the *o*-Me protons versus just the one seen for each of the Ru(TMP)L$_2$ species (L = MeCN, MeSSM) (Figure 6). Integration of the resonances in the *o*-Me region furnishes a distribution diagram for the Ru species, and a calculated K_2/K_1 ratio of 2.0 ± 0.4 (Table S2, Figure 7). The cooperative effect ($K_2 > K_1$) is consistent with the nondetection of a μ-MeSSMe species even at a low [MeSSMe]; indeed, the bis-MeSSMe species is observed even at a MeSSMe:Ru mol ratio of 0.42 (Figures 5, 6, S3 and S4, spectrum 2; Table S2, entry 2). More standard behavior ($K_2 < K_1$) is exemplified by an unhindered Rh(porp)(I)/MeSSMe reaction that only forms a mono-adduct,[53] and by Co^{II}–porphyrin systems in noncoordinating solvents.[59] More intriguing is the similar $K_2 < K_1$ behavior of Fe^{II} porphyrin systems, which is usually ascribed to the gain in crystal field stabilization energy on going from a high-spin, five-coordinate species to a low-spin six-coordinate species;[12a,60] in contrast, the Ru^{II}–porphyrin species here are six-coordinate, low-spin. However, K_2/K_1 is typically in the 10–30 range for Fe porphyrin species[60] compared to ~2 in the Ru(TMP)–MeCN–MeSSMe system, where metal–ligand interactions such as the relative *trans* influence of MeSSMe and MeCN in the mixed ligand species might be important. The greater polarizing power of S- versus N-containing ligands in platinum metal complexes,[47] and the greater basicity of MeSSMe versus

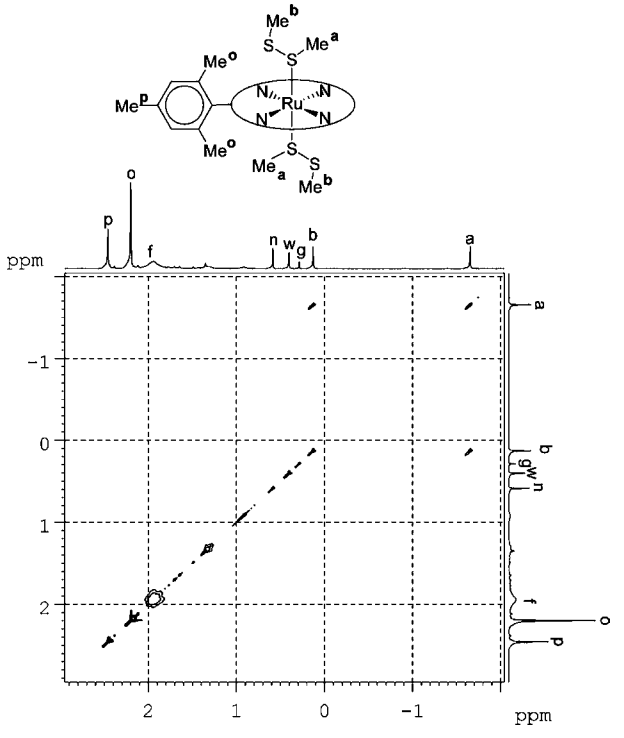


Figure 4. ^{1}H–^{1}H EXSY NMR spectrum (300 MHz, C_6D_6) of in situ sample of Ru(TMP)(MeSSMe)$_2$. Assignments: a, b, o, p, see schematic diagram (top); f, free MeSSMe; n, free MeCN; w, residual H_2O; g (see Figure 1 legend).

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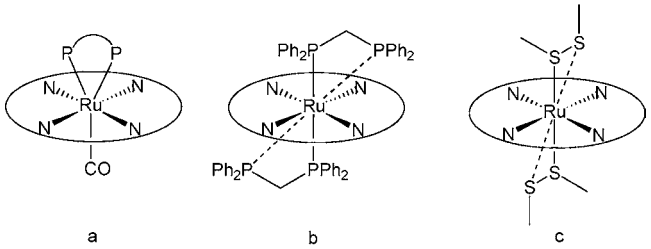
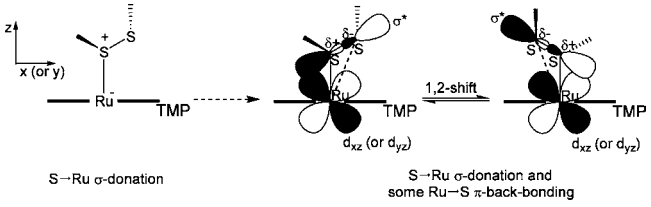
Chart 6. Plausible Seven- and Eight-Coordinate Ru(porphyrin) Species



$(\overset{\frown}{P\ \ P} = Ph_2P(CH_2)_2PPh_2)$

Scheme 4. π-Back-Bonding to the Disulfide $\sigma^*_{(S-S)}$ Orbital



MeCN (at least in the gas phase),[61] coupled with the fact that ligand substitution reactions of Ru(TMP)L_2 complexes (L = nitriles, amines, imines) occur via a dissociative (or interchange dissociative) mechanism,[62] likely favor the substitution reaction of eq 7 (vs eq 6) and result in a higher K_2 value (relative to K_1).

3.4. Bis-Trisulfide Complexes. Whereas the organic chemistry of trisulfides, particularly with regard to biological and medicinal properties, is well-documented,[63] reports on their coordination chemistry are scarce.[64] Many naturally occurring trisulfides have been isolated, or prepared in situ, during workup procedures of plant, algae, ascidia, or fungi extracts,[63] but the metabolic/physiologic functions in these organisms are not well-defined.[63d] The natural products calichemicin and esperamicin, for instance, inaugurate a new class of potent antitumor antibiotics,[65a,b] with mechanisms depending upon a complex chain of reactions triggered by a trisulfide moiety that cleaves DNA.[65c,d] The cytotoxicity of varacin, a cyclic pentasulfide natural

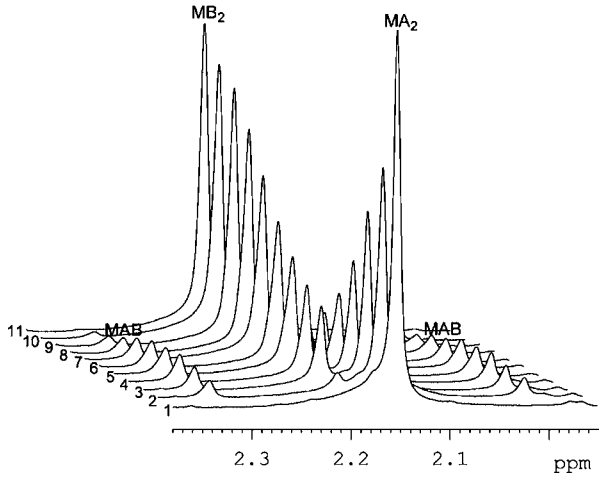


Figure 6. ^{1}H NMR spectra (mesityl *o*-Me region) for the Ru(TMP)$(MeCN)_2$/MeSSMe titration (300 MHz, C_6D_6 ; Table S2); M = Ru(TMP); A = MeCN; B = MeSSMe.

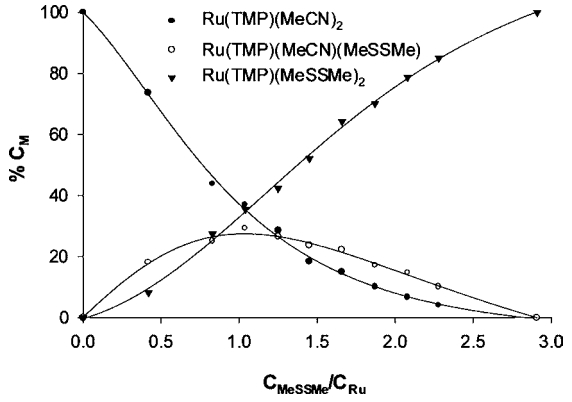


Figure 7. Species distribution diagram for the Ru(TMP)MeCN/MeSSMe system; data in Table S2 (C_M = concentration of species).

product, has been ascribed to radical, oxidative DNA damage (via Fenton-like chemistry), and derivatization to a trisulfide species possibly plays a key role in the biological activity.[66] Studies on such

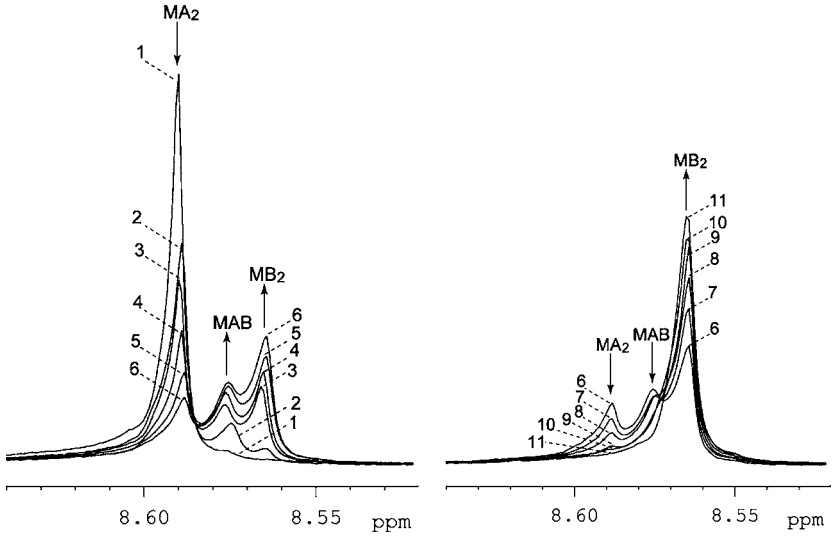


Figure 5. ^{1}H NMR spectra (β-pyrrole region) for the Ru(TMP)$(MeCN)_2$/MeSSMe titration (300 MHz, C_6D_6 ; Table S2); M = Ru(TMP); A = MeCN; B = MeSSMe.

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activity of garlic and onion organosulfur compounds are also relevant here, in that their extracts are rich in diallyl trisulfide that has anticarcinogenic and antiproliferative activity in which modulation of cytochrome P450 activity has been implicated.[67,68] However, details of the trisulfide–hemoprotein interactions remain unknown.

Our studies on the trisulfide complexes of Ru porphyrins were limited to the commercially available RSSSR (R = Me or Bn). The in situ syntheses of the Ru(porp)$(RSSSR)_2$ complexes were akin to those of the thiol, sulfide and disulfide species. The two singlets or two sets of ^{1}H NMR signals seen for the coordinated RSSSR moieties of Ru(porp)$(MeSSSMe)_2$ and Ru(porp)$(BnSSSBn)_2$, respectively, reveal nonsymmetric coordination of the trisulfide. The R group closest to the porphyrin plane again experiences a more pronounced ring-current shielding effect; the NMR data thus imply coordination to a terminal rather than a central S atom since the latter would give only one set of proton signal(s) for both R groups of an RSSSR ligand. The possibility of an η^2-1,2-coordination mode of RSSSR cannot be completely excluded, but an end-on η^1-mode is assigned by analogy to data for the disulfide systems. Theoretical calculations on trisulfides favor η^1-coordination through the terminal sulfur,[64g] but coordination via the central S atom can be forced by incorporating the trisulfide into an appropriate chelating ligand.[64c] The suggested coordination of nontethered trisulfides to Pt^{II} via the central sulfur in early work remains speculative.[64d,e]

Of interest, remarkable linear correlations are observed between the ring-current shielding shifts for the axial-ligand C^1 proton(s) of the Ru(porp)$(RS_xR)_2$ complexes (x = 1–3) and x (Table 6, Figure 8). For the MeS_xMe series, an increase in x gives a decrease in $\Delta\delta_H$ for both TMP and T-*p*Me-*PP* systems, with respective slopes of −0.09 and −0.12 ppm/S atom. Conversely, corresponding $\Delta\delta_H$ values in the BnS_xBn series increase linearly with x (+0.16 and +0.12 ppm/S atom). The poorer correlation seen for the Ru(TMP)$(BnS_xBn)_2$ series may result from interactions of the benzyls with the mesityl *o*-Me groups of TMP (see below).

Rationales for these correlations are unclear within the steric and electronic effects that must control the ligand coordination but, assuming that the shielding reflects the proximity of the C^1H to the porphyrin ring and thus the "strength" of the Ru–S interaction, the conclusions would be that the interaction of MeS_xMe decreases in the order sulfide > disulfide > trisulfide. If steric effects in the MeS_xMe species are negligible, the trend could mirror the donor strength of the ligands and, consistent with this, the stability constant for binding of MeSMe to cytochrome P450 adduct is double that of MeSSMe.[19] For the BnS_xBn series, steric effects could override electronic effects and, as a benzyl group is much more sterically demanding than a S atom,[58a] the extension of the S-chain in the BnS_xBn series could reduce steric congestion and allow for better coordination and the observed trend: trisulfide > disulfide > sulfide. Related is the nonbonding interaction between the Ph groups and porphyrin ring within Ru(OEP)$(PhSPh)_2$, which is reflected in both solid state characteristics and solution chemistry of this complex.[4b] The same trend seen for the BnS_xBn species has also been established within a crystalline polymeric network formed by coordination of diallyl trisulfide, disulfide, and sulfide to CuCl, where bonding of the allyl moieties was also verified.[64j] Of note, these diallyl compounds (present in garlic) modulate the activity of P450 (again in the same trisulfide > disulfide > sulfide order),[68b] and their toxicity also follows the same trend.[69a] A tentative conclusion is that dibenzyl derivatives might be better structural models for the diallyl compounds than the dimethyl series. In the P450 systems,[68] protein–substrate interactions are almost certainly involved as well as heme–sulfur binding.

Of the garlic-derived RS_xR compounds (x = 1–3; R = alkyls, allyl) that show biological activitiy,[69] the dialkyls are largely ineffective,[68f,69c,f] whereas the diallyl species, particularly the trisulfide,[68f,69] show high hepatoprotectivity against CCl_4-induced hepatotocixity,[68f] antiproliferative activity against cancer cell lines,[69c,e–g] and antimicrobial activity.[69a,b,d] A recent systematic study has revealed that trisulfides of hindered dialkenyl series are invariably more active than those of the alkyl series.[69g] The "conceived" resemblance between the structural dependence of these biological systems and that discussed for the Ru(porp)$(RS_xR)_2$ systems might be purely incidental, and in-depth studies on both biological and biomimetic fronts are clearly needed.

The linear correlations of Figure 8 bring to mind the findings that the molecular refractive indicies, logarithms of viscosity, and chromatographic capacity factors, within the homologous

Table 6. Ring-Current Effects for Ru(porp)L_2 Species (L = Sulfide, Trisulfide).[a,b,c]

		$\Delta\delta_H = \delta_H$ (free L) − δ_H (coordinated L)			
Ru(porp)	L	C^1H ($C^{1\prime}H$)	*o*-*H*-Ph (*o*-*H*-Ph′)	*m*-*H*-Ph (*m*-*H*-Ph′)	*p*-*H*-Ph (*p*-*H*-Ph′)
Ru(TMP)	MeSMe	3.75	–	–	–
	MeSSSMe	3.51	–	–	–
		(1.28)	–	–	–
	BnSBn	3.77	1.83	0.84	0.71
	BnSSSBn	4.09	1.35	0.65	0.65
		(1.72)	(0.76)	(0.31)	(0.31)
Ru(T-*p*Me-*PP*)	MeSMe	3.96	–	–	–
	MeSSSMe	3.78	–	–	–
		(1.32)	–	–	–
	BnSBn	3.93	1.95	0.75	0.62
	BnSSSBn	4.17	1.52	0.71	0.61
		(1.41)	(0.71)	(0.25)	(0.25)

[a] δ values in ppm (C_6D_6). [b] Data for the RSSR-disulfide species (R = Me, Bn) are given in Table 5. [c] Data for free sulfides and trisulfides are given in Table S1.

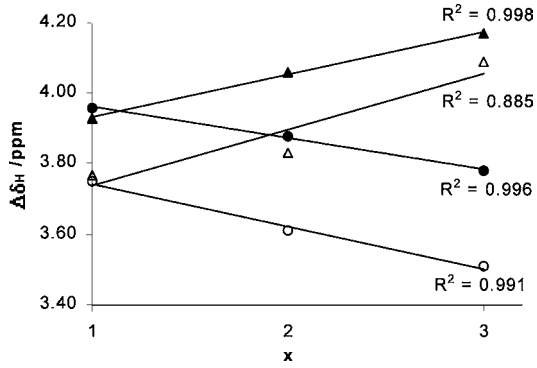

Figure 8. Ring-current shielding shifts for C^1H of the RS_xR ligands (x = 1–3; R = Me or Bn): ○ Ru(TMP)$(MeS_xMe)_2$; ● Ru(T-*p*Me-*PP*)$(MeS_xMe)_2$; △ Ru(TMP)$(BnS_xBn)_2$;▲ Ru(T-*p*Me-*PP*)-$(BnS_xBn)_2$. Standard deviations are smaller than the size of the symbols.

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RS_xR series ($x \geq 1$) are reportedly also linear functions of the number of S atoms in the polysulfide chain,[63c,70]

3.5. Reactions with H_2S. Preliminary studies on the reaction of H_2S with benzene solutions of Ru(TMP)(MeCN)$_2$ have provided no evidence for formation of an H_2S adduct; elemental analyses and MS data of isolated, but as yet unpurifed, products are more consistent with formation of a dimeric species with a (TMP)RuSSRu(TMP) core. Work continues on the H_2S reactions.

4. CONCLUSIONS

Ruthenium(II)−porphyrin complexes with bis-thiol, -sulfide, -disulfide, and -trisulfide axial ligands are readily prepared from Ru(porp)(MeCN)$_2$. The ^{1}H NMR data are the first reported for any metalloporphyrin complexes with axial thiol ligands, and reveal upfield shifts for the S*H* protons because of the porphyrin π-ring current. The bis-thiol complexes represent potential models for recently proposed short-lived thiol-(cysteine)-bound, low-spin six-coordinate Fe^{II} species thought to participate in heme protein-mediated processes (see Introduction). Exchange of the MeCN ligands with a disulfide ligand is sensitive to the nature of the disulfide: the primary disulfide MeSSMe gives Ru(TMP)(RSSR)$_2$ (R = Me), the tertiary ^{t}BuSS^{t}Bu is unreactive, and MeSS^{t}Bu coordinates via the less sterically hindered S atom. The R = Me species has η^1-*S* disulfide ligands with geometry reminiscent of that of bis(sulfide) and bis(*S*-sulfoxide) analogues, and undergoes 1,2-Ru−S-metallotropic shifts in solution at room temperature. The bis(disulfide) species is formed in successive solution equilibria via Ru(TMP)(MeCN)(MeSSMe) that are characterized by a cooperative effect ($K_2/K_1 \approx 2.0$). This is ascribed to the relative *trans* effects of MeSSMe and MeCN in the mixed ligand species; this contrasts with a similar but larger cooperativity effect seen in Fe^{II}−porphyrin systems, which results from gain in crystal field stabilization energy. By analogy to the disulfide species, the Ru(porp)(RSSSR)$_2$ complexes (R = Me, Bn) are thought to contain η^1-coordinated trisulfides via a terminal S atom. Analysis of noteworthy linear correlations between the ring-current shielding shifts for the axial-ligand C^1 protons of the Ru(porp)$(RS_xR)_2$ systems (R = Me, Bn, x = 1−3) and x suggests that the species may be of relevance as models for studying the biological effects of diallyl trisulfide, where interactions with P450 have been implicated.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

CIF for Ru(TMP)(MeSSMe)$_2$·2C$_6$H$_6$; ^{1}H−^{1}H COSY NMR spectra of Ru(porp)(^{n}PrSS^{n}Pr)$_2$ (porp = TMP and T-*p*Me-*PP*); ^{1}H NMR data for free thiols, sulfides, disulfides, and trisulfides in C$_6$D$_6$; and experimental data for the ^{1}H NMR titration of Ru(TMP)(MeCN)$_2$ with MeSSMe. This material is available free of charge via the Internet at http://pubs.acs.org.

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