

It can be noted that the study presented here not only clarifies the mechanism of the back-extraction of NiL_2 with copper(II) ion but also validates the extraction technique for the kinetic examination of metal-exchange reactions of water-insoluble chelates.

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Electron Transfer. 59. Reactions of Pyrazine-Related Radicals and Dihydro Species with Metal-Center Oxidants¹

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The reductions of various substituted pyrazines and quinoxalines, using V^{2+} or Eu^{2+} in strongly acid media, yield long-lived colored aromatic radicals. With phenazines, reductants in deficiency give radicals whereas an excess of reductant brings about transfer of a second electron to form the corresponding dihydro aromatics. In the case of 1-deazariboflavin (IV), the radical is observed only as a transient species (λ_{max} 665 nm), which is converted rapidly to the dihydro derivative. The specific rates for most of these conversions, when carried out with V^{2+} , are great enough to ensure that they occur mainly by outer-sphere paths. Reduction of the 1-deazaflavin to its radical appears to be catalyzed by the dihydro compound. The patterns of specific rates for oxidation of the pyrazinium and quinoxalium radicals with halopentaamminecobalt(III) complexes indicate that these conversions also utilize an outer-sphere path, a conclusion confirmed in one instance by characterization of the oxidation product as the parent heterocycle with the ring system unhalogenated. Phenazinium radicals are found to react inconveniently slowly with substitution-inert cobalt(III) complexes but measurably rapidly with a number of substitution-labile metal-center oxidants. The observed acidity dependence for oxidation of the *N*-methylphenazinium radical by Fe^{3+} is consistent with the intervention of an *N*-bound $\text{Fe}(\text{III})$ -radical precursor. As observed in flavin-related systems, the dihydro derivatives of the phenazines are more rapid reductants than the corresponding radicals. The acid dependencies for the reactions of these dihydro compounds (and of the dihydro derivatives of riboflavin and 1-deazariboflavin as well) with a series of $(\text{NH}_3)_5\text{Co}^{\text{III}}$ complexes point to partition of each of these reductants between an active basic form and an inactive acidic form with a $\text{p}K_{\text{a}}$ value in the range 0.4–1.0. In these reductions there is no acceleration attributable to carboxyl bridging nor any rate enhancements resulting from extension of conjugation in the ligand; we are thus dealing again with outer-sphere processes. log–log plots comparing the reactivities of any two of these dihydro reductants are linear with near-unit slope, in accordance with the model of Marcus. Analogous plots comparing specific rates for a dihydro derivative with those for reduction by $\text{Ru}(\text{NH}_3)_6^{2+}$ exhibit severe scatter, with $\text{Ru}(\text{II})$ reductions of $(\text{NH}_3)_5\text{CoCl}^{2+}$ and the complexes of α -keto acids proceeding unexpectedly rapidly. Attempted $\text{Eu}(\text{II})$ reduction of 5-deazariboflavin (VII), in which the pyrazine-like system has been disrupted, yields colorless solutions containing only small steady-state concentrations of the corresponding radical. This deazaflavin, unlike its 1-deaza isomer, catalyzes the reductions, by Eu^{2+} , of $\text{Co}(\text{NH}_3)_5\text{py}^{3+}$ and $\text{Co}(\text{en})_3^{3+}$.

Electron-transfer processes involving pyrazine-related systems have received a spate of recent and detailed attention. A number of research groups have examined ligated pyrazines in their role as mediators of charge transfer between metal ion centers,² whereas the prominence of flavins (which are fused-ring derivatives of pyrazine) as oxidation coenzymes has prompted a multitude of studies of the function which they serve in controlling organic oxidations *in vitro*.³ Ancillary areas of investigation are the electrochemistry of pyrazine species⁴ and the transformations of metal-bound pyrazine radicals.⁵ The recognized richness of the chemistry of pyrazines reflects, in large part, the presence of the two donor

centers lying in conjugation in the ring, the ease with which many derivatives undergo separable and reversible 1- and 2-electron reduction, and the persistence of certain pyrazine-related radicals in solution near room temperature.

The present paper deals with the reduction of several substituted pyrazines in aqueous solution at high acidity to the related radicals or dihydro derivatives and with the reactions of these reduced species with a variety of metal-center oxidants.

Experimental Section

Materials. Solutions of the perchlorates of $\text{Eu}(\text{II})^{6a}$ and $\text{V}(\text{II})^{6bc}$ were prepared as described. Master solutions of $\text{UO}_2(\text{ClO}_4)_2$, $\text{Fe}(\text{ClO}_4)_3$, and $\text{Cu}(\text{ClO}_4)_2$ were prepared from the hydrated perchlorates (Alfa) and were standardized spectrophotometrically as described.⁷ Quinoxaline (Aldrich) was purified by fractional freezing. Samples of 1-deazariboflavin^{8a} and 5-deazariboflavin^{8b} were generously supplied

- (1) Support of this work by the National Science Foundation (Grant 8022881) is gratefully acknowledged.
- (2) See, for example: (a) Malin, J. M.; Ryan, D. A.; O'Halloran, T. V. *J. Am. Chem. Soc.* **1978**, *100*, 2097. (b) Haddad, M. S.; Hendrickson, D. N.; Cannady, J. P.; Drago, R. S.; Bieksza, D. S. *Ibid.* **1979**, *101*, 898. (c) Von Kameke, A.; Tom, G. M.; Taube, H. *Inorg. Chem.* **1978**, *17*, 1790. (d) Johnson, E. C.; Callahan, R. W.; Ickberg, R. P.; Hatfield, W. E.; Meyer, T. J. *Ibid.* **1979**, *18*, 618.
- (3) For recent reviews, see: (a) Hemmerich, P. *Adv. Chem. Ser.* **1977**, No. 162, 312. (b) Walsh, C. *Ann. Rev. Biochem.* **1978**, *47*, 881. (c) Bruice, T. C. *Acc. Chem. Res.* **1980**, *13*, 256.
- (4) (a) Klatt, L. N.; Rouseff, R. L. *J. Am. Chem. Soc.* **1972**, *94*, 7295. (b) Swartz, J.; Anson, F. C. *Inorg. Chem.* **1981**, *20*, 2250.
- (5) (a) Dunne, T. G.; Hurst, J. K. *Inorg. Chem.* **1980**, *19*, 1152. (b) Wu, M.-Y.; Paton, S. J.; Fanchiang, Y.-T.; Gelerinter, E.; Gould, E. S. *Ibid.* **1978**, *17*, 326.

- (6) (a) Dockal, E. R.; Gould, E. S. *J. Am. Chem. Soc.* **1972**, *94*, 6673. (b) Guenther, P. R.; Linck, R. G. *Ibid.* **1971**, *93*, 2769. (c) Linck, R. G. *Inorg. Chem.* **1970**, *9*, 2529.
- (7) "IUPAC Spectrometric Data"; Butterworths: London, 1963; pp 149 (Cu^{II}), 223 (Fe^{III}), 550 (UO_2^{2+}).
- (8) (a) 1-Deazariboflavin, prepared by the procedure of Ashton and co-workers (Ashton, W. T.; Graham, D. W.; Brown, R. D.; Rogers, E. F. *Tetrahedron Lett.* **1977**, *30*, 2551) was donated by the Research Laboratories of Merck Sharp and Dohme. We are grateful to Dr. W. T. Ashton for arranging transfer of this sample. (b) 5-Deazariboflavin was obtained through the courtesy of Dr. C. C. Cheng of the Mid-America Cancer Center with the authorization of the Drug Synthesis and Chemistry Branch of the National Cancer Institute.

by investigators at other institutions. Additional heterocyclic reactants were Aldrich products and were used as received.⁹ Cobalt(III) complexes were available from previous studies.^{5b,10}

Generation of Radicals and Dihydro Derivatives. Radicals and dihydro species were prepared in solution by treatment of solutions of their parent aromatics in 1.0 M HClO₄ with measured quantities of V²⁺ or Eu²⁺. All preparations and reactions were carried out under nitrogen. Quinoxalines and monocyclic pyrazines were converted smoothly to their radicals with 1 equiv or less of reductant, but excess V²⁺ or Eu²⁺ converted the radical to the 2-electron-reduction product, the dihydro species, which, in these instances, appeared to undergo some irreversible decomposition. In such systems, reactions of the radical, but not those of the dihydro derivative, were examined. With the phenazines, both the radical and the dihydro compound could be made to persist at appropriate levels of reductant, and experiments with both reduced species could be carried out. In the case of 1-deazariboflavin, although the radical could be observed (*vide infra*), disproportionation kept its concentration low under our conditions, and reactions of only the dihydro compound were studied.

Treatment of 5-deazariboflavin with an excess of V²⁺ or Eu²⁺ resulted in no alteration of spectra attributable to formation of a radical or a dihydro species. However, solutions of this deazaflavin in 1.2 M HClO₄ were found to catalyze the Eu²⁺ reductions of Co(NH₃)₅py³⁺ and Co(en)₃³⁺, thus indicating^{10b} a small degree of conversion to a strongly reducing radical in this medium. Observed catalytic activities were comparable to those reported for 4-pyridineacrylic acid^{10b} under comparable conditions.

Rate Measurements. Rates of formation of the various reduced pyrazine species and their reactions with metal-center oxidants were estimated from absorbance changes on a Cary 14 recording spectrophotometer or a Durrum-Gibson stop-flow spectrophotometer.¹¹ Conversions of monocyclic pyrazines and substituted quinoxalines to their radicals were followed on the Cary at the visible absorption maxima for the radicals, keeping the reductant, V²⁺, in deficiency. Reductions of the phenazines and 1-deazariboflavin were studied on the Durrum with V²⁺ in excess. Oxidations of the generated radicals were generally monitored at the maxima of the metal-center oxidants. Oxidations of the dihydro compounds were followed by measuring the rate of appearance of the colored radicals in the phenazine systems or the parent aromatic (formed by disproportionation of the radical) in the deazaflavin system. As in earlier studies of dihydroriboflavin,^{10c} the dihydro species used in kinetic runs were generated by using excess V²⁺ or Eu²⁺, waiting until the first traces of colored heterocyclic oxidation product (reflecting slow leakage of O₂) appeared, and then adding the oxidant.¹²

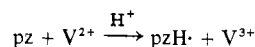
Reactions were first order in both oxidant and heterocyclic reductant but were carried out under pseudo-first-order conditions with one of the two reactants in greater than 10-fold excess. When the effect of acidity was being examined, the concentration of added HClO₄ was allowed to vary while the total ionic strength was maintained near 1.2 M by adding thrice-recrystallized LiClO₄. Reactions were generally followed for at least 4 half-lives. Rate constants obtained from successive half-life values within a run agreed to within 6%, whereas specific rates from replicate runs checked to better than 9%. Temperatures were kept at 25.0 ± 0.2 °C during all runs on the Cary and 20.5 ± 0.5 °C for runs on the Durrum.

Identification of Product. A solution in which 2,3-dimethylquinoxalinium radical was generated from equivalent quantities of the parent heterocycle and V(ClO₄)₂ in 1.2 M HClO₄ was allowed to react with an equimolar quantity of (NH₃)₅CoBr(ClO₄)₂ for 30 min. The mixture was brought to pH 8 by addition of Na₂CO₃ and extracted with ether, and the UV spectrum of the ether extract was

Table I. Radicals Derived from Substituted Pyrazines and Quinoxalines

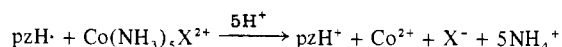
| radical | color | λ_{\max} , nm | ϵ^a | k_V^b |
|---------------------------------------------------------------------------|--------|-----------------------|-----------------------|-----------------------|
| pyrazinium (I, R = H) | purple | 565 | 28 | 30 |
| methylpyrazinium (I, R = 2-CH ₃) | blue | 590 | 28 | 20 |
| 2,5-dimethylpyrazinium (I, R = 2,5-Me ₂) | purple | 570 | 30 | 27 |
| 2,6-dimethylpyrazinium (I, R = 2,6-Me ₂) | purple | 570 | 28 | 20 |
| quinoxalinium (II, R = H) ^c | yellow | 357 | 1.4 × 10 ⁴ | 1.7 × 10 ³ |
| 2,3-dimethylquinoxalinium (II, R = 2,3-Me ₂) | yellow | 370 | 1.1 × 10 ⁴ | 7.0 × 10 ² |
| 2,3-dicarboxypyrazinium (I, R = 2,3-(COOH) ₂) | yellow | 680 | 43 | 11 |
| 2,3-dicarbamoylpyrazinium (I, R = 2,3-(CONH ₂) ₂) | yellow | 440 | 40 | 18 |

^a Molar absorptivity, M⁻¹ cm⁻¹. ^b Specific rates (M⁻¹ s⁻¹) for formation of radical from the parent heterocycle:



Reactions were carried out at 25 °C in 1.2 M HClO₄. ^c See ref 11a.

Table II. Specific Rates for Oxidation of Pyrazine- and Quinoxaline-Related Radicals with Halopentaamminecobalt(III) Complexes, Co(NH₃)₅X²⁺



| radical | k^a | | |
|----------------------------|--------|-----------------------|-----------------------|
| | X = Cl | X = Br | X = I |
| pyrazinium | 1.9 | 32 | 1.1 × 10 ² |
| methylpyrazinium | 9.8 | 2.2 × 10 ² | 7.0 × 10 ² |
| 2,5-dimethylpyrazinium | | 4.6 × 10 ² | 2.1 × 10 ³ |
| 2,6-dimethylpyrazinium | | 4.7 × 10 ² | 2.6 × 10 ³ |
| quinoxalinium ^b | 0.69 | 8.3 | 54 |
| 2,3-dimethylquinoxalinium | 16 | 4.0 × 10 ² | |

^a Specific rates (M⁻¹ s⁻¹) at 25 °C; reaction medium was 1.2 M HClO₄. Rates were not dependent on acidity in the [H⁺] range 0.2–1.2 M. ^b Specific rates for the reactions of this more stable radical (see ref 11a) with (NH₃)₅CoF²⁺ (0.2 M⁻¹ s⁻¹) and with (NH₃)₅CoN₃²⁺ (0.48 M⁻¹ s⁻¹) could be estimated.

taken. This spectrum corresponded to that of the original heterocyclic base.

Results and Discussion

Visible absorption maxima for radicals derived from various substituted pyrazines (I) and quinoxalines (II) are listed in

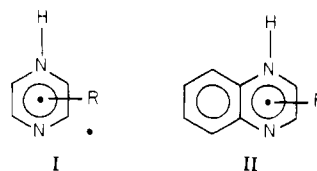


Table I, together with specific rates for generation of these radicals via reduction with V²⁺ (k_V values). For the pyrazinium radicals, k_V 's are seen to fall below 40 M⁻¹ s⁻¹, the substitution-controlled upper limit for inner-sphere reductions by this reagent under the conditions used,¹³ and are thus compatible with the operation of either an inner- or outer-sphere path (or a combination of both) in these instances. Specific rates for formation of the quinoxalinium radicals

- (9) Solutions of phenazine methosulfate, which are photosensitive, were stored in flasks wrapped in aluminum foil.
- (10) (a) Fan, F.-R. F.; Gould, E. S. *Inorg. Chem.*, **1974**, *13*, 2639. (b) Fanchiang, Y.-T.; Carlson, R. R.; Thamburaj, P. K.; Gould, E. S. *J. Am. Chem. Soc.* **1977**, *99*, 1073. (c) Singh, A. N.; Srinivasan, V. S.; Gould, E. S. *Inorg. Chem.* **1982**, *21*, 1236.
- (11) (a) Chang, C.-R.; Paton, S. J.; Gelerinter, E.; Gould, E. S. *Inorg. Chem.* **1979**, *18*, 1294. (b) Singh, A. N.; Gelerinter, E.; Gould, E. S. *Ibid.* **1982**, *21*, 1232.
- (12) When this procedure was used, oxidation of the dihydro compound by adventitious oxygen was negligible in comparison to reaction with the added oxidant. We were unable to obtain satisfactory data for these systems when reactions were run in 10-cm cells (reaction volume ca. 28 cm³).

- (13) (a) Hicks, K. W.; Toppen, D. L.; Linck, R. G. *Inorg. Chem.* **1972**, *11*, 310. (b) Chen, J. C.; Gould, E. S. *J. Am. Chem. Soc.* **1973**, *95*, 5539. (c) Sutin, N. *Acc. Chem. Res.* **1968**, *1*, 225.

Table III. Electronic Spectra of the Reduced Forms of Aromatic Heterocyclic Series and Specific Rates for Their Formation

| | λ_{\max} , nm (ϵ^a) | $10^{-4}k_V^b$ |
|-------------------------------------------------------|---------------------------------------------------------------------------------------------------------|----------------|
| phenazine ^c | | |
| parent aromatic radical | 450 sh (1.6), 426 (2.5), 382 (23), 364 sh (13), 276 sh (2.0), 255 (74) | |
| radical | 636 (1.3), 586 sh (0.9), 443 (10.7), 432 (8.0), 370 (6.0), 308 (1.5), 255 (53), 252 sh (51) | 6.5 |
| dihydro species | 300 sh (7.1), 273 (11), 243 (18) | 3.2 |
| <i>N</i> -methylphenazine (III, R = CH ₃) | | |
| parent aromatic radical | 464 sh (2.0), 434 (3.2), 387 (29), 370 sh (15), 268 (92) | |
| radical | 644 (1.4), 594 sh (1.0), 460 sh (8.0), 445 (11), 434 sh (10), 370 (7.9), 310 (4.3), 290 (2.2), 256 (52) | 21 |
| dihydro species | 300 sh (7.5), 268 (17), 245 (12) | 5.0 |
| 1-deazariboflavin (IV) | | |
| parent aromatic radical ^d | 520 (9.3), 372 (5.2), 304 (61), 265 sh (26), 231 (50) | |
| radical ^d | 665 (>2.1) | 1.0 |
| dihydro species | 341 (17), 276 (27), 238 sh (34) | 7 |

^a ϵ values in $M^{-1} \text{ cm}^{-1} \times 10^{-3}$; sh = shoulder; medium 1.2 M HClO₄. ^b Specific rates for formation by 1-electron reduction using V²⁺, $M^{-1} \text{ s}^{-1}$ (20 °C, 1.20 M HClO₄). ^c N-Protonated form. ^d Unstable species (see text); only one absorbance peak detected.

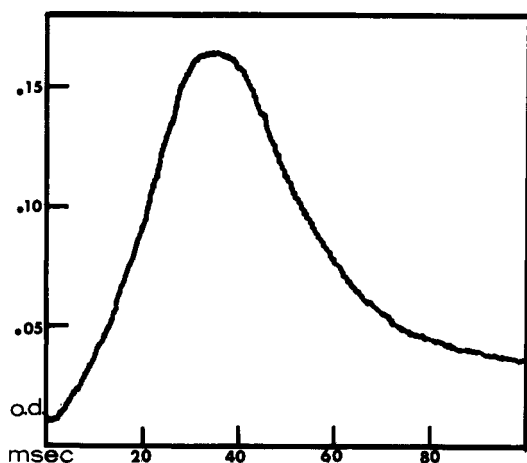


Figure 1. Kinetic profile of the reduction of 1-deazariboflavin (IV) ($3.9 \times 10^{-5} \text{ M}$) with V(ClO₄)₂ ($6.2 \times 10^{-4} \text{ M}$) in 1.2 M HClO₄, showing the formation and destruction of the radical. The reaction was carried out at 20 °C and $\mu = 1.2$, with $\lambda = 665 \text{ nm}$, mixing time 5 ms, and optical path length 2.0 cm. Note the acceleration of the reaction during its early stages, pointing to autocatalysis. The observed curve is consistent with a sequence in which the flavin, Ar, is reduced to the radical, ArH• ($k = 5.7 \text{ s}^{-1}$), and then to the dihydro derivative, ArH₂ ($k = 43 \text{ s}^{-1}$), after which ArH₂ reacts rapidly with Ar to form 2 ArH• (see text).

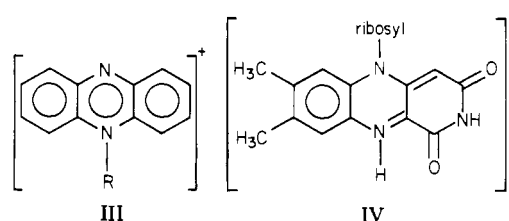
greatly exceed this limit, however, and therefore point strongly to the predominance of an outer-sphere route in these cases and, if uniformity of mechanism is assumed, for the pyrazinium radicals as well.

An earlier report^{11a} alluded to the slow decomposition of the quinoxalium radical under conditions similar to those employed in this study. Decomposition of pyrazinium radicals, for which Klatt^{4a} has proposed a path involving degradation of the ring, is significantly more severe and militates against carrying out kinetic studies of the reactions of such radicals with sluggish oxidants. Table II, however, gives specific rates for the reactions of several of the radicals with (NH₃)₅CoCl²⁺, (NH₃)₅CoBr²⁺, and (NH₃)₅CoI²⁺, three of the most rapidly reduced of the known pentaamminecobalt(III) species.¹⁴ These rates appear to be independent of acidity in the range 0.2–1.2 M H⁺.

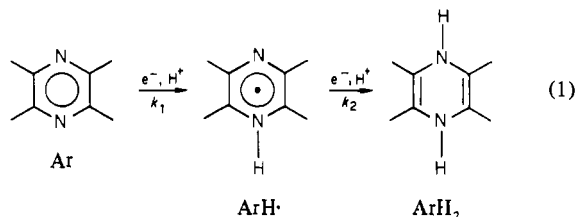
Ratios of specific rates, k_1/k_{Cl} , pertaining to reactions of the radicals with iodo- and chlorocobalt(III) complexes, fall between 60 and 80, quite close to the corresponding ratio (40) reported^{14c} for reductions by Ru(NH₃)₆²⁺ (an outer-sphere

reductant), but substantially greater than the analogous ratios for Cr²⁺ (5.0)^{14b} (the prototype inner-sphere reductant) and for V²⁺ (15.8)^{6bc} (which probably uses both routes). The difference in selectivity suggests an outer-sphere route for oxidations of the radicals, and this path is confirmed by characterization of the product from reaction of the dimethylquinoxalium radical and the bromo oxidant as the parent heterocycle with the ring system apparently un-brominated.^{15,16}

Kinetic profiles for the reactions of phenazine (III, R = H),



the *N*-methylphenazine ion (III, R = CH₃), and 1-deazariboflavin (IV) with excess V²⁺ in 1.2 M HClO₄ show the formation of the respective radicals and their subsequent conversion, by further reduction, to the corresponding dihydro species (ArH₂) (see eq 1). The curves observed in the



phenazine-related systems may be resolved into two consecutive pseudo-first-order components leading to the rate constants 6.5×10^4 and $3.2 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ for the two stages of reduction of the protonated form of phenazine and 2.1×10^5 and $5.0 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ for the corresponding reductions of methylated

(14) (a) Candlin, J. P.; Halpern, J.; Trimm, D. L. *J. Am. Chem. Soc.* **1964**, *86*, 1019. (b) Candlin, J. P.; Halpern, J. *Inorg. Chem.* **1965**, *4*, 766. (c) Endicott, J. F.; Taube, H. *J. Am. Chem. Soc.* **1964**, *86*, 1686.

(15) A reviewer has reminded us of a number of inner-sphere reductions in which the bridging ligand is *not* transferred to the reductant but instead remains bound to the oxidant (in its reduced form).¹⁶ We note, however, that each of these involves an oxidant derived from a second- or third-row transition metal (e.g. Ru^{III} or Ir^{IV}), which, upon reduction, yields a substitution-inert center. In our systems, the reduction product, a Co^{II} species, is highly substitution labile, and any bridged intermediate featuring a C–Br–Co^{II} linkage would undoubtedly undergo heterolysis at Co^{II}.

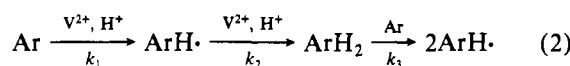
(16) See, for example: (a) Taube, H.; Myers, H. *J. Am. Chem. Soc.* **1954**, *77*, 2103. (b) Thornley, R. N. F.; Sykes, A. G. *J. Chem. Soc.* **1970**, 232. (c) Grossman, B.; Haim, A. *J. Am. Chem. Soc.* **1970**, *92*, 4835. (d) Movius, W. G.; Linck, R. G. *Ibid.* **1969**, *91*, 5394. (e) Seewald, D.; Sutin, N.; Watkins, K. O. *Ibid.* **1969**, *91*, 7307.

Table IV. Kinetic Data for Reactions of the *N*-Methylphenazinium Radical with Thallium(III) and with Iron(III)^a

| Tl(III) oxidant | | Fe(III) oxidant | |
|----------------------|-------------------------------------------------------------|----------------------|-------------------------------------------------------------|
| [H ⁺], M | 10 ⁻² <i>k</i> , M ⁻¹ s ⁻¹ | [H ⁺], M | 10 ⁻² <i>k</i> , M ⁻¹ s ⁻¹ |
| 0.0014 | 5.6 | 0.0014 | 45 |
| 0.20 | 5.0 | 0.20 | 34 |
| 0.40 | 5.3 | 0.40 | 29 |
| 0.60 | 5.0 | 0.60 | 24 |
| 0.80 | 5.1 | 0.80 | 22 |
| 1.20 | 4.7 | 1.20 | 18.0 |

^a Reactions were carried out at 25 °C and $\mu = 1.20$ (HClO₄ + NaClO₄). Radicals were generated by treatment of 10⁻⁵ M phenazine methosulfate with a deficiency of V²⁺ or Eu²⁺. Initial ratio [oxidant]/[radical] = 6–20. Reactions were followed at 445 nm (see Experimental Section).

phenazine.^{17–19} The profile for reduction of the deazaflavin (Figure 1), recorded at 665 nm (the visible maximum for the radical), points to a more complicated picture. Early in the reaction, the rate of formation of the radical is seen to increase with time, demonstrating autocatalysis and indicating the operation of sequence 2 in which *k*₁ and *k*₂, pertaining to



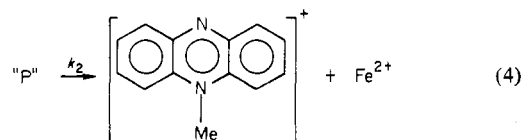
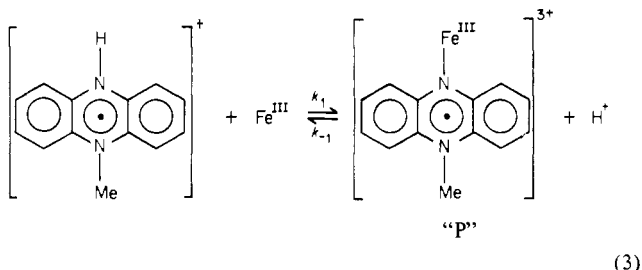
electron transfer between a metal center and an aromatic system, are each much less than *k*₃, which applies to transfer between two aromatics. Analysis of the curve shown during the final 25% of decay of ArH[•] (when [Ar] is very nearly zero) allows us to estimate *k*₂ as 43 s⁻¹, whereas the extrapolation of the slope during the early stages of reaction to zero time yields a *k*₁ value near 6 s⁻¹.²⁰ These parameters lead to second-order rate constants (20 °C, $\mu = 1.2$) 1 × 10⁴ and 7 × 10⁴ M⁻¹ s⁻¹ for the V²⁺ reductions of the deazaflavin and its radical. In this instance, in contrast to what is observed in the riboflavin^{11b} and phenazine systems, *k*₂ > *k*₁, reflecting the relative instability of the 1-electron-reduction product. Spectral characteristics of the phenazines and the deazaflavin are compared with those of their respective reduction products in Table III.

The elusive nature of the radical derived from 1-deaza-riboflavin complicates the study of its reactions with added oxidants. At the other extreme, the radicals derived from the phenazines may be handled with ease in aqueous acidic so-

lutions, but their oxidations by substitution-inert cobalt(III) complexes are found to be inconveniently slow. Reactions with a number of the substitution-labile metal-center oxidants are more rapid; we have explored several of these in a preliminary fashion.

Table IV summarizes kinetic data for the reaction of the *N*-methylphenazinium radical with Tl³⁺ and Fe³⁺. Rates with Tl³⁺ are seen to be independent of acidity in the range [H⁺] = 0.0014–1.2 M, whereas the Fe³⁺ reaction is retarded at high acidities but approaches a limiting rate at low. The latter pattern suggests a system in which one of the reactants is partitioned into an unreactive acidic form and a kinetically active basic form, with the two forms existing in comparable concentrations when [H⁺] lies near 0.5 M. However, the partitioned reactant cannot be Fe(H₂O)₆³⁺ (p*K*_A = 3.0),²¹ nor is it the radical (for the protonation equilibrium is seen to play no part in its reaction with Tl³⁺).

We therefore favor, for the oxidation by Fe³⁺, a path featuring the intervention of a Fe(III)-radical precursor (designated "P"), formed with loss of H⁺, after which electron transfer occurs:



Applying the steady-state approximation to precursor P leads to rate law 5. Although experiments under steady-state

$$\text{rate} = \frac{[\text{Fe}^{\text{III}}][\text{MePh}\cdot]k_1k_2}{k_{-1}[\text{H}^+] + k_2} \quad (5)$$

conditions do not allow evaluation of all three rate constants, a plot of (rate/[Fe^{III}][MePh[•]])⁻¹ vs. [H⁺], which is closely linear, gives 1/*k*₁ as intercept and *k*₋₁/*k*₁*k*₂ as slope, leading to *k*₁ = 4.4 × 10³ M⁻¹ s⁻¹ and *k*₂/*k*₋₁ = 0.49 M.^{22,23}

The oxidation by Tl³⁺, a 2-electron reagent, requires successive acts of electron transfer from two aromatic radicals. The first of these steps, producing the unstable state Tl²⁺, may, in analogy to known noncomplementary Tl(III) reductions,²⁴ be considered as rate determining. Intervention of a precursor

(17) See, for example: Frost, A. A.; Pearson, R. G., "Kinetics and Mechanism", 2nd ed.; Wiley: New York, 1961, p 167. As several authors have pointed out,¹⁸ any kinetic profile reflecting the formation and destruction of an absorbing intermediate by sequential first- or pseudo-first-order processes can be resolved into two pairs of transformations having the same numerical values for their specific rates, but with reversed sequence. In both both of the systems treated here, the greater specific rate was assigned to the initial reaction by computing the maximum degree of conversion to the radical,¹⁶ estimating its extinction coefficient, and comparing its value with that observed in static experiments (Table III). Analogous treatment of the reverse sequences yielded apparent extinction coefficients of the radical which were several times greater than the observed values.

(18) See, for example: (a) Alcock, N. W.; Denton, D. J.; Moore, P. *Trans. Faraday Soc.* **1970**, *66*, 2210. (b) Espenson, J. H. "Chemical Kinetics and Reaction Mechanisms"; McGraw-Hill: New York, 1981; p 69.

(19) Note again that each of these specific rates greatly exceeds the substitution-controlled limit for inner-sphere reductions by V²⁺.¹³

(20) Early in this reaction, when the degree of conversion of the parent flavin is low, the steady-state approximation may be applied to ArH₂, which, if [V²⁺] is considered to be very nearly constant leads to

$$d[\text{ArH}\cdot]/dt = k_1a + (k_2 - k_1)x$$

where *a* is the initial concentration of Ar and *x* is the quantity reduced. In the range that this equation holds, a plot of reaction rate vs. *x* yields, as slope, the difference *k*₂ - *k*₁. The value so obtained 35 s⁻¹, is in agreement with the values of *k*₁ and *k*₂ obtained by considering the reaction in its initial and final stages.

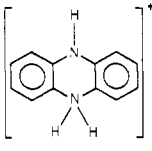
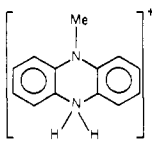
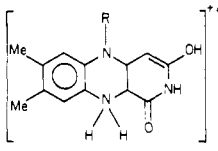
(21) Smith, R. M.; Martell, A. E., "Critical Stability Constants"; Plenum Press: New York, 1976; Vol. 4, pp 7, 11.

(22) The most questionable aspect of the sequence proposed for oxidation of the methylphenazinium radical by Fe(III) is the relatively low value for *k*₁, the specific rate for ligand substitution at a high-spin d⁵ center. Contrary to the general view that substitution reactions at metal centers in aqueous solutions are measurable by conventional mixing techniques only when activation entails a significant loss in ligand field stabilization, there are an increasing number of reports²³ of measurably slow substitutions at metal centers which are conventionally taken to be substitution labile.

(23) See, for example: (a) Birk, J. P. *Inorg. Chem.* **1975**, *14*, 1724. (b) Thompson, G. A. K.; Sykes, A. G. *Ibid.* **1976**, *15*, 638. (c) Dash, A. C.; Nanda, R. K. *Ibid.* **1973**, *12*, 2024. (d) Paquette, G.; Zador, M. *Inorg. Chim. Acta* **1978**, *26*, L23. (e) Martin, A. H.; Gould, E. S. *Inorg. Chem.* **1976**, *15*, 1934.

(24) See, for example: (a) Ashurst, K. G.; Higginson, W. C. E. *J. Chem. Soc.* **1953**, 3044. (b) Higginson, W. C. E.; Rosseinsky, D. R.; Stead, J. B.; Sykes, A. G. *Discuss. Faraday Soc.* **1960**, *29*, 49.

Table V. Representative Kinetic Data for Reactions of Dihydro Derivatives of Phenazines and 1-Deazariboflavin with Cobalt(III) Oxidants^a

| oxidant | reductant | [H ⁺], M | 10 ⁻² k _{obsd} ^b | 10 ⁻² k _{calcd} ^c |
|-------------------------------------------------------|-----------------------------------------------------------------------------------|----------------------|-------------------------------------------------|--------------------------------------------------|
| (NH ₃) ₅ CoF ²⁺ |  | 0.10 | 1.38 | 1.39 |
| | | 0.30 | 0.69 | 0.70 |
| | | 0.50 | 0.46 | 0.47 |
| | | 0.70 | 0.34 | 0.36 |
| | | 0.90 | 0.28 | 0.28 |
| | | 1.10 | 0.24 | 0.23 |
| | | 1.30 | 0.21 | 0.20 |
| (NH ₃) ₅ Co(py) ³⁺ |  | 0.10 | 3.7 | 3.7 |
| | | 0.30 | 2.6 | 2.6 |
| | | 0.50 | 2.0 | 2.0 |
| | | 0.70 | 1.60 | 1.60 |
| | | 0.90 | 1.34 | 1.35 |
| | | 1.10 | 1.15 | 1.16 |
| | | 1.30 | 0.99 | 1.02 |
| (NH ₃) ₅ Co(OAc) ²⁺ |  | 0.10 | 0.37 | 0.36 |
| | | 0.30 | 0.150 | 0.187 |
| | | 0.50 | 0.125 | 0.127 |
| | | 0.70 | 0.110 | 0.096 |
| | | 0.90 | 0.095 | 0.077 |
| | | 1.10 | 0.079 | 0.064 |
| | | 1.30 | 0.069 | 0.055 |

^a Reactions were carried out at 25.0 °C with $\mu = 1.30$, $[\text{reductant}]_0 = 3 \times 10^{-5} - 1 \times 10^{-4}$ M, and $[\text{oxidant}] = 5 \times 10^{-4} - 2 \times 10^{-3}$ M. ^b k values in $\text{M}^{-1} \text{s}^{-1}$. ^c Values calculated as $k_{\text{lim}}K_{\text{HA}}(K_{\text{HA}} + [\text{H}^+])^{-1}$; parameters k_{lim} and K_{HA} for each reaction are listed in Table VI. ^d R = ribosyl.

similar to that suggested for Fe(III) is reasonable, but the strongly acidic character of Ti^{3+} ($\text{p}K_{\text{A}} = 1.0$)²¹ would be expected to minimize reversal of precursor formation (k_{-1}), resulting in the acid-independent rates observed for this oxidant.²⁵

As observed in flavin-related systems,^{10c,11b} the dihydro derivatives of the phenazines are generally more rapid reductants than the corresponding phenazinium radicals. The reactions of the dihydrophenazines, and of the dihydro derivative of 1-deazariboflavin as well, with substitution-inert cobalt(III) oxidants are strongly acid dependent; typical data appear in Table V. Rates with all three dihydro compounds conform to eq 6, which characterizes a system in which the

$$k = I_{\text{lim}}K_{\text{HA}}/(K_{\text{HA}} + [\text{H}^+]) \quad (6)$$

oxidant or reductant is distributed between a basic form, reacting at a limiting specific rate, k_{lim} , and an unreactive protonated form having an acidity constant K_{HA} . Values of parameters k_{lim} and K_{HA} giving the closest agreement between observed specific rates and rates calculated by (6) are summarized in Table VI. The K_{HA} values pertaining to the various reductions by a given dihydro compound are seen to be nearly the same; moreover, none of the cobalt(III) complexes has a proton that is removable near the acidity range studied. We therefore infer that the dihydro species are undergoing partial deprotonation with the K_{HA} values listed and that the respective protonated forms have negligible reactivity under our conditions.

Since the distribution of the reductant between protonation levels is independent of the Co(III) complex with which it reacts, the limiting specific rates, pertaining to reaction of additional oxidants with each of the dihydro compounds in its nonprotonated form, may be calculated from measurements at a single acidity. Table VII lists measured specific rates and calculated limiting values for the reactions of various

Table VI. Kinetic Parameters for Acid-Dependent Reactions of Cobalt(III) Complexes with the Dihydro Derivatives of Phenazines and 1-Deazariboflavin

| reductant ^a | oxidant ^b | k_{lim}^c | K_{HA}^c |
|------------------------|------------------------------------------------------|--------------------|-------------------|
| PhH_3^+ | Ro(pyruvato) ²⁺ | 82.7 ± 5.0 | 0.125 ± 0.007 |
| | Ro(imidazole) ³⁺ | 291 ± 17 | 0.102 ± 0.007 |
| | RoF ²⁺ | 273 ± 16 | 0.100 ± 0.007 |
| | Ro(bimaleato) ²⁺ | 607 ± 36 | 0.100 ± 0.012 |
| | av | 0.107 | |
| PhMeH_2^+ | Ro(trimethylacetato) ²⁺ | 44.8 ± 2.7 | 0.55 ± 0.03 |
| | Ro(bimaleato) ²⁺ | 91.4 ± 6.4 | 0.38 ± 0.04 |
| | Ro(dimethylformamide) ³⁺ | 397 ± 26 | 0.40 ± 0.02 |
| | Ro(py) ³⁺ | 477 ± 28 | 0.35 ± 0.03 |
| | av | 0.42 | |
| DzRbH_3^+ | Ro(py) ³⁺ | 56 ± 7 | 0.11 ± 0.03 |
| | Ro(acetato) ²⁺ | 67 ± 12 | 0.12 ± 0.03 |
| | RoCl ²⁺ | 87 ± 8 | 0.15 ± 0.02 |
| | Ro(<i>N,N</i> -dimethyl-nicotinamide) ³⁺ | 99 ± 11 | 0.14 ± 0.03 |
| | UO ₂ ²⁺ | 89 ± 12 | 0.12 ± 0.03 |
| | av | 0.13 | |

^a For structural formulas of the reductants, see Table V.

^b Ro = "roseo" = (NH₃)₅Co^{III}. ^c The parameters k_{lim} and K_{HA} appear in eq 6. Values in the table were obtained by nonlinear least-squares refinement of unweighted kinetic data by minimizing $(k_{\text{obsd}} - k_{\text{calcd}})^2$.

(NH₃)₅Co^{III} complexes with the three dihydro reductants and includes, for comparison, the limiting values^{10a} for reductions by dihydroriboflavin (RbH₂).

Although there are differences in detail, the reactivity patterns for the three dihydro derivatives resemble each other closely and are, at the same time, similar to the selectivity pattern observed for dihydroriboflavin.^{10c} With the three dihydro species, and with RbH₂ as well, the (carboxylato)-cobalt(III) derivatives examined are reduced at rates quite near those for the complexes of pyridine, imidazole, and pyrazine, which are considered to be typical outer-sphere oxidants.^{13b,26} Thus, there is no significant acceleration attributable to bridging by the carboxyl ligand. Moreover the pronounced rate enhancements resulting from incorporation of α -carbonyl

(25) Further exploratory experiments indicate that specific rates (25 °C, 1.2 M HClO₄) for oxidation of the *N*-methylphenazinium radical by Fe(*bpy*)₃³⁺ ($2.1 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$) and by Ce(IV) ($2 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$) lie near the upper limit of the range measurable by conventional mixing techniques, whereas the oxidation of the phenazinium radical by Cu(II) ($k = 5.3 \text{ M s}^{-1}$) is considerably slower. Acid dependencies for these reactions have not yet been determined.

(26) Fan, F.-R. F.; Gould, E. S. *Inorg. Chem.* 1974, 13, 2647.

Table VII. Specific Rates for Oxidations of the Dihydro Derivatives of Phenazines and 1-Deazariboflavin with Pentaamminecobalt(III) Complexes, $R(NH_3)_5Co^{III}$

| ligand, R | $k(PhH_3^+)$ | | $k(PhMeH_2^+)$ | | $k(DzRbH_3^+)$ | | $k(RbH_3^+)$ lim ^c |
|----------------------------------|-------------------|--------------------------------|-------------------|--------------------------------|-------------------|-------------------|----------------------------------|
| | obsd ^a | lim ^b | obsd ^a | lim ^b | obsd ^a | lim ^b | |
| ethylenediamine ^d | 1.02 | 13.2 | 1.21 | 5.0 | 0.13 | 1.4 | 2.3 |
| ammonia | 2.4 | 31 | 2.9 | 11.9 | 0.53 | 5.8 | |
| imidazole | 22 | 2.9×10^2 ^e | 15.0 | 61 | 4.5 | 50 | 41 |
| pyrazole | 115 | 1.5×10^3 | 83 | 3.5×10^2 | 5.0 | 55 | 160 |
| pyridine | 169 | 2.2×10^3 | 105 | 4.7×10^2 ^e | 5.5 | 56 ^e | 156 |
| <i>N,N</i> -dimethylformamide | 136 | 1.8×10^3 | 102 | 3.9×10^2 ^e | 5.2 | 56 | 2.5×10^2 |
| aquo | | | 3.3×10^2 | 1.4×10^3 | 7.1 | 78 | 5.5×10^2 |
| <i>N,N</i> -dimethylnicotinamide | | | 4.8×10^2 | 1.9×10^3 | 10.4 | 99 ^e | 6.0×10^2 |
| benzonitrile | | | | | 19 | 2.1×10^2 | |
| triethylacetato | 23 | 2.9×10^2 | 13 | 53 | | | |
| trimethylacetato | 33 | 4.3×10^2 | 14.4 | 59 | 6.8 | 75 | |
| acetato | 140 | 1.8×10^3 | 68 | 2.7×10^2 | 6.8 | 67 ^e | |
| formato | 51 | 6.7×10^2 | 22 | 90 | 4.0 | 44 | 187 |
| propionato | 141 | | | | 7.5 | 83 | |
| pyruvato | 7.5 | 83 ^e | 5.7 | 23 | | | |
| phenylglyoxylato | 35 | 4.6×10^2 | 17.3 | 71 | 4.9 | 54 | 121 |
| bimaleato | 44 | 6.1×10^2 ^e | 21 | 91 ^e | | | 88 |
| fluoro | 22 | 2.7×10^2 ^e | 21 | 86 | 6.0 | 66 | 36 |
| chloro | | | 173 | 7.1×10^2 | 9.8 | 87 ^e | 170 |
| bromo | | | | | 125 | 1.4×10^3 | |
| iodo | | | | | 4.9×10^2 | 5.3×10^3 | |
| azido | | | | | 9.4 | 104 | 2.5×10^2 |
| UO_2^{2+} ^f | | | 104 | 4.3×10^2 | 9.1 | 89 ^e | |

^a Specific rates ($M^{-1} s^{-1}$) for reactions at 25 °C in 1.3 M $HClO_4$. Structural formulas for the reductants are given in Table V. ^b Limiting specific rates calculated, unless otherwise indicated, as $k_{lim} = k_{obsd} (1 + [H^+]/K_{HA})$, where $[H^+]$ is 1.3 M and average values of K_{HA} for the reductants are given in Table VI. ^c Values from ref 10c. ^d $Co(en)_3^{3+}$. ^e Values obtained from nonlinear least-squares refinement of kinetic data (see Table VI). ^f Reactions of UO_2^{2+} with $PhMeH_2^+$ and with $DzRbH_3^+$ were found to follow the same type of rate law as the cobalt(III) complexes in the table.

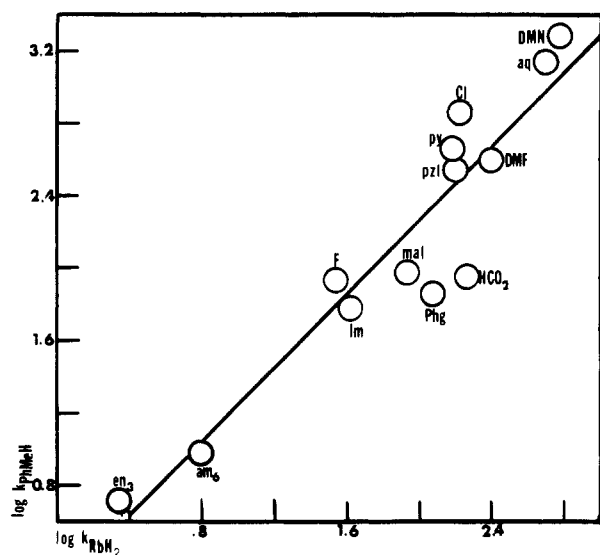


Figure 2. log-log plot comparing the specific rates of reduction of pentaamminecobalt(III) complexes, $R(NH_3)_5Co^{III}$, by the dihydro derivatives of *N*-methylphenazine ($PhMeH$) and riboflavin (RbH_2). Both sets are limiting values at low acidities (Table VII). am_6 = hexaammine; im = imidazole; mal = bimaleato; Phg = phenylglyoxylato; pzl = pyrazole; DMN = *N,N*-dimethylnicotinamide. The regression line shown corresponds to the equation $\log k(PhMeH) = 1.03 \log k(RbH_2) + 0.20$.

functions in inner-sphere series^{10a,27} do not appear here. The absence of specific substituent effects then indicates that we are again dealing with outer-sphere processes.

A corollary of Marcus's model²⁸ for adiabatic outer-sphere electron-transfer reactions is that when two different reductants

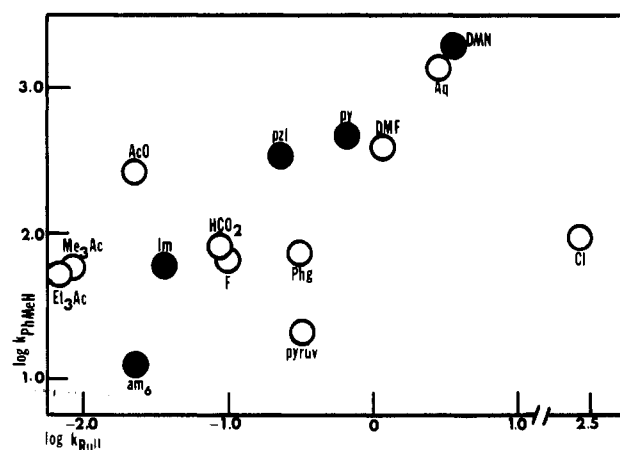


Figure 3. log-log plot comparing the specific rates of reduction of pentaamminecobalt(III) complexes, $R(NH_3)_5Co^{III}$, by $(NH_3)_6Co^{II+}$ ($\mu = 0.50$, supporting electrolyte $LiCl$) and by the deprotonated form of the dihydro derivative of *N*-methylphenazine ($PhMeH$). $pyruv$ = pyruvato; the remaining abbreviations are those used for Figure 2. The abscissa has been compressed between 1.0 and 2.5. Solid circles designate $(NH_3)_5Co^{III}$ derivatives of *N*-donor ligands (see text).

react with the same series of oxidants, the ratio of rate constants should remain very nearly constant throughout the series, i.e., that log-log plots comparing the reactivities of the two reductants should be linear with unit slope. The outer-sphere reactions of $(NH_3)_5Co^{III}$ derivatives with several metal-center reductants (Cr^{2+} , Eu^{2+} , $Ru(NH_3)_6^{2+}$, V^{2+} , and U^{3+}) have been found to adhere to this picture,^{6a,10a,13b,26,29} and the corresponding plot comparing reductions by the dihydro derivatives of riboflavin and *N*-methylphenazine (Figure 2), although exhibiting some scatter, is seen also to approach linearity with near-unit slope.

(27) (a) Taube, H.; Gould, E. S. *Acc. Chem. Res.* **1969**, *2*, 321. (b) Zanella, A.; Taube, H. *J. Am. Chem. Soc.* **1972**, *94*, 6403. (c) Gould, E. S. *Ibid.* **1974**, *96*, 2373.

(28) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155.

(29) Loar, M. K.; Sens, M. A.; Loar, G. W.; Gould, E. S. *Inorg. Chem.* **1978**, *17*, 330.

