CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY,
ILLINOIS INSTITUTE OF TECHNOLOGY, CHICAGO, ILLINOIS 60616

Strain Energy Minimization and Conformational Analysis of Cobalt(III) Complexes with the Flexible Tetramine Ligand *N,N'*-Bis(2-picolyl)-1,2(*S*)-propanediamine

BY GEORGE R. BRUBAKER* AND RICHARD A. EULER

Received September 22, 1971

Strain energy minimization calculations have been performed on several of the possible s-cis and uns-cis isomers of the complex ions diacido- or oxalato(*N,N'*-bis(2-picolyl)-1,2(*S*)-propanediaminecobalt(III) for the purpose of establishing the source of the stereospecific coordination of the flexible tetramine ligand. The strain energy of the Δ uns-cis isomers is at least 3 kcal/mol less than that calculated for the Λ isomers, while the strain energies of the Δ (or Λ) isomers differ by only about 10% (0.9 kcal/mol). Valence angle deformation and rotation about the propanediamine C–C bond provide the largest contributions to the strain energy in our model.

We have recently reported details of the synthesis, resolution, and properties of the oxalato, malonato, and some diacido complexes of cobalt(III) with *N,N'*-bis(2-picolyl)-1,2-propanediamine (picpn).[1] Stereospecific coordination of the ligand picpn was demonstrated by comparison of the optical rotation of the ligand prepared *via* an asymmetric synthesis with that of the ligand isolated from the resolved complex. Spectroscopic evidence strongly indicates that the first formed isomer is the uns-cis, contrary to an earlier report of preferential formation of the s-cis isomer.[2] Among the uns-cis isomers, our earlier spectroscopic results[1] indicated that only the Δ-*uns-cis*-[Co(*S*-picpn)X_2]$^+$ isomer is formed for a variety of unidentate anionic ligands, X^-. In addition, we reported the apparent isomerization of the *uns-cis*-[Co(picpn)ox]$^+$ ion to the corresponding s-cis topology in the solid state as well as in solution. Conformational analysis of some of the isomers of diacido and oxalato picpn complexes was undertaken to confirm our interpretation of the spectroscopic data.

Hawkins has written an excellent review of the technique of conformational analysis.[3] Much of the current application of these techniques to coordination compounds stems from the general availability of an energy minimization program written by Boyd. The program and the mathematical method have been described in detail elsewhere.[4,5] We wish to present, through examples, some comments on the method which we believe will help a novice to use the program or, more properly, to evaluate its output.

Method

Trial Coordinates.—We obtained our initial coordinate set directly from photographs of scaled molecular models. We find that the "bond distortions" of flexible framework models actually locate the atoms quite close to the equilibrium positions. We prepare "Polaroid" lantern slides of appropriate views of a model and of a coordinate grid. When both images are projected simultaneously, we find that we can obtain a complete coordinate set within about 1 hr. While we recognize that this function can be performed by a computer, our method is about as fast as typical computer center turnaround times. Invariant internal coordinates were chosen as described by Buckingham, *et al.*[5]

Interactions.—We obtain significant interactions from a careful study of scaled molecular models. Our pictorial method, while relatively slow, has an obvious advantage over computer searching. As we search for interactions, we bend the models to account for interactions which are significant for a given conformation, and also for those interactions which become significant only after a shift of the molecular coordinates. These latter nonbonded interactions may be considered as somewhat of a restoring force. They are not found in a typical computer search which seeks a range of contact distances for each conformation.

The program writes the total strain energy as the unweighted sum of all of the energy contributions from the individual interactions. For this reason, we deem it essential to hold the number and kind of interactions as nearly constant as practicable for each of the series of isomers to be compared. Excluding the oxalate dianion, 185 interactions were considered. When the oxalate dianion was included, 223 interactions were employed.

The unstrained condition for each interaction must be specified, *i.e.*, unstrained bond lengths, angles, and contact distances. Experimental values for bond lengths, contact distances, and valence angles are generally available. Torsional angles of minimum energy are not as easily specified; in general, we extrapolate from related alicyclic systems, and accept the staggered conformation as lowest in energy.

The "rigidity" of the energy minimum, or the energy required to achieve a unit displacement from the minimum energy angle or distance, must also be specified. For bond length and valence angle deformation, spectroscopic force constants provide a measure of this "rigidity." For nonbonded interactions and torsional barriers, the "rigidity" is not as clearly defined, and we resort to constants taken from the literature as applied in similar studies. In general, these constants are not experimentally determined, and are quite inexact. Unfortunately, bond twisting and nonbonded interactions are often the most significant factors in a conformational analysis, and the choice of parameters frequently determines the equilibrium coordinates.

---

[1] J. Cragel, Jr., and G. R. Brubaker, *Inorg. Chem.*, **11**, 303 (1972).

[2] B. Bosnich, *Proc. Roy. Soc., Ser. A*, **297**, 88 (1967).

[3] C. J. Hawkins, "Absolute Configuration of Metal Complexes," Wiley-Interscience, New York, N. Y., 1971.

[4] R. H. Boyd, *J. Chem. Phys.*, **49**, 2574 (1968).

[5] D. A. Buckingham, I. E. Maxwell, A. M. Sargeson, and M. R. Snow, *J. Amer. Chem. Soc.*, **92**, 3617 (1970).

TABLE I

FINAL ENERGY TERMS (KCAL/MOL) FROM MINIMIZATION

	Complex							
	a	b	c	d	e	f	b (ox)	c (ox)
Bond deformation	0.27	0.23	0.31	0.23	0.26	0.25	0.34	0.43
Nonbonded interactions	0.99	0.64	0.85	1.50	1.27	0.34	0.45	0.85
Valence angle distortion	6.99	6.12	6.71	7.87	10.41	6.55	9.02	9.56
Torsion	1.94	2.24	3.29	3.50	2.60	1.80	2.24	3.29
Total	10.19	9.24	11.16	13.11	14.55	8.94	12.06	14.13

For complex molecules, the force field can always be adjusted to reduce or eliminate any unusual features which appear in the output of the energy minimization scheme. These adjustments usually comprise one good fit for another. For example, it is possible to fix constants which will hold the coordination sphere of the metal ion perfectly rigid, thereby demanding distortions in the coordinated ligands.

Hawkins[3] has carefully listed interaction constants and the assumptions implicit in each of the published sets. We have used the interaction constants of Snow[6] and of Buckingham, *et al.*,[5] without exhaustive or critical evaluation. For the pyridine nuclei, we have used Boyd's benzenoid constants.[4] In this study, we recognize that our potential functions are probably incorrect. We believe that we can ignore errors in the choice of potential functions for comparison of a group of isomers minimized under the same set of assumptions *if* there are no indications that the energy minimization scheme has altered the molecule beyond intuition and experience.

Computation.—All calculations were performed on the IIT Univac 1108 system using a locally modified version of Boyd's energy minimization program.

Output.—The basic Boyd program produces a list of input atomic coordinates, interactions, and interaction constants, a list of the interactions and the strain energy associated with each, a list of new atom coordinates, the total strain energy as the sum of the contributions from each interaction, and the root mean squared coordinate shifts accepted as a criterion for convergence. A subroutine is included for the calculation of vapor-phase thermodynamic functions and vibrational frequencies.

Results and Discussion

There are two possible s-cis isomers for our model compound, namely Δ-[Co(*S*-picpn)X_2]$^+$ and Λ-[Co(*S*-picpn)X_2]$^+$. An examination of molecular models suggests that the interaction between the methyl substituent and the picolyl methylene group should mitigate against formation of the Δ isomer. Both of these isomers were included in the energy minimization study. The uns-cis isomers chosen for strain energy minimization were those which may be converted to one or the other of the s-cis topologies *via* a simple trigonal shift but without exchange of a secondary amine proton. These conditions are imposed by the nature of the tetramine which prohibits exercise of any other intramolecular rearrangement mechanism, and by our observation that isomerization occurs both in acidic solution and in the solid state where proton exchange is seemingly unlikely.

Initially, strain energy minimization was performed on a model which included only the metal ion and the *S*-picpn ligand. Subsequently, we included the oxalato dianion to complete the strain energy minimization for the lowest lying uns-cis isomer and the most closely related s-cis complex. Internal bond lengths and angles for the oxalato dianion were taken from the literature.[7] The coordinated oxygen atoms were described as nominally trigonal (*i.e.*, the unstrained Co–O–C angle was set to 120°) in keeping with the multiple bond character of the oxalate chelate ring. After several cycles, this angle was reduced to about 110° involving about 0.8 kcal/mol of strain energy. There is no other significant contribution to the strain energy within the oxalate ion. Including the strain in the O–Co–O angle, *our model* of the oxalate ion contributes about 2.9 kcal/mol to the strain energy of each complex. From this experience, we conclude that it is reasonable to ignore the fifth- and sixth-coordination positions on the metal ion while searching the tetramine for the source of its stereospecificity.

Criteria for Convergence.—The basic program provides for termination of the iteration sequence either after a set number of iterations or after the rms shift of the coordinates falls below a prescribed limit, whichever occurs first in the course of a calculation. Typically, the rms shift at convergence is set to less than 0.01 Å. After several cycles of iteration, we found that the rms shift did not converge below about 0.05 Å, even though our version of the program is equipped with a damping factor as described by Buckingham.[5] For this study, another feature of our program proved extremely useful. At the end of each run, a set of final coordinates is punched for possible use as input to subsequent runs. Thus we can interrupt our calculation sequence at any point to examine the course of the calculation.

After about eight iterations, the calculation was terminated, and the interactions and coordinate shifts carefully examined. None of the bond lengths were distorted beyond accepted limits, as demonstrated by the uniformly low value for the total bond length deformation energy (Table I). None of the angles within the coordination sphere appear to be distorted beyond crystallographically determined limits, and the angles within the aliphatic linkages are close to 109°; none of the distortions contributes excessively to the total energy for the group (Table I). The model we have used effectively constrains the pyridine nucleus to a plane, and there are no significant distortions from these planes.

There are two significant contributors to the total strain energy; one is stereochemically significant, and the other apparently contributes only to the high rms shifts in the final cycles of iteration. Careful examina-

---

(6) M. R. Snow, *J. Amer. Chem. Soc.*, **92**, 3617 (1970).

(7) In our model, input coordinates for the oxalato dianion were those of F. R. Ahmed and D. W. J. Cruickshank, *Acta Crystallogr.*, **6**, 385 (1953). The calculated coordinates are quite similar to those found by Lethbridge, *et al.*, in a recent structural study of some oxalato complexes (*J. Chem. Soc. A*, 1862 (1970)).

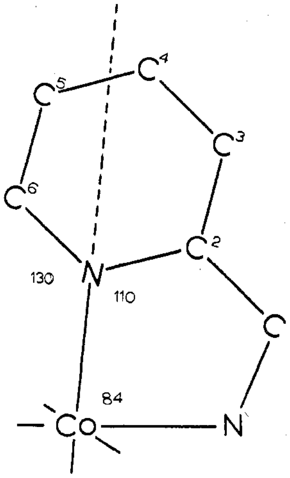

Figure 1.

tion of the large contributors to the strain energy showed that the angles about the pyridine nitrogen atoms are significantly distorted. The angle Co–pyN–pyC(6) is about 130°, the angle Co–pyN–pyC(2) is about 110°, and the internal angle is about 120° in each case. Physically, the angular distortion corresponds to the terminal chelate ring pulling the pyridine nitrogen atom away from an axis joining the metal ion, the pyridine nitrogen, and the 4-carbon of the pyridine ring (Figure 1). Accordingly, the N–Co–N angle in the terminal chelate ring is reduced to about 84°. In *our model*, the program rocks the pyridine nucleus as a unit in an attempt to minimize the distortions about the pyridine nitrogen atom. In successive iterations, we find the 4-carbon of the pyridine nuclei shifted by nearly 0.5 Å along an axis normal to the plane of the ring; the 3- and 5-carbon atoms are shifted in the same direction by about 0.2 Å, and the 2- and 6-carbons by about 0.08 Å. The sign of the shift changes on each cycle, and the magnitude of the shift does not decrease through at least four cycles. Addition of the oxalate dianion in the final cycles did not effect the convergence of the pyridine nuclei, in agreement with the expected small interaction between the coordinated oxalate and the pyridine rings.

Coordinate shifts in all other atoms including the pyridine nitrogens are less than the rms shift for the molecule as a whole. The relatively large rms shift at convergence is thus seen to be a consequence of coordinate shifts of ten atoms which are not significant in determining the stereospecificity of the ligand. We must emphasize that these results are a consequence of the model we have chosen to represent the Co–N bond, the pyridine ring, the pyridine nitrogen atom, and the barrier to rotation about the picolyl ring substituent. The barriers to distortion of the pyridine nitrogen and cobalt valence angles are comparable in magnitude; the pyridine ring is effectively rigid, and the barrier to rotation about the bond joining the pyridine 2-carbon and the substituent methylene group is negligible as in toluene.

Stereospecificity.—Once we established to our satisfaction that the strain energy minimization calculation had converged, we turned our attention to the energy differences which give rise to stereospecific coordination.

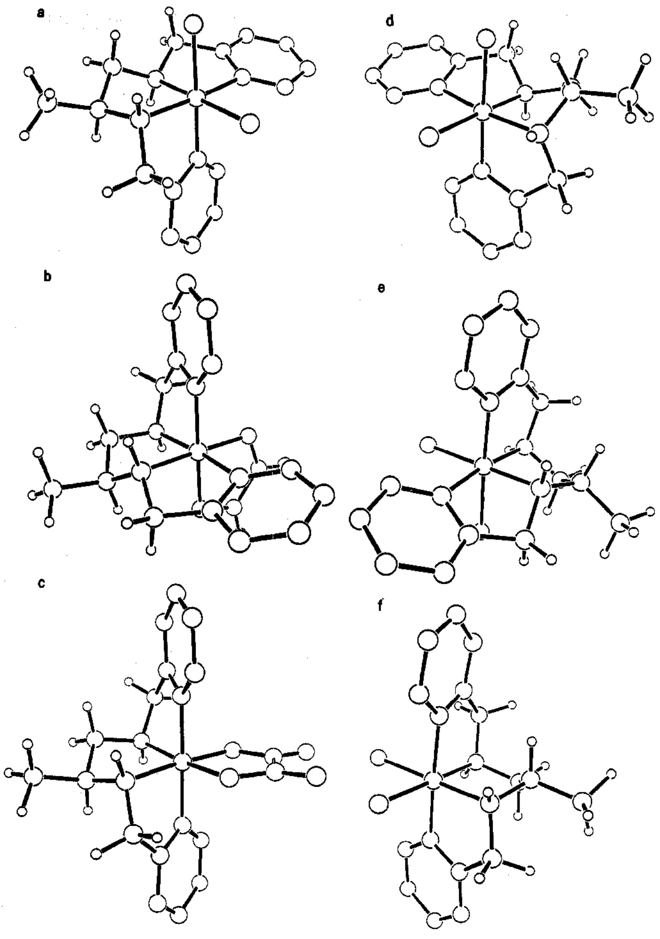

Figure 2.

We have only concerned ourselves with strain energy differences among the uns-cis isomers as calculated neglecting the influence of the oxalate ligand (*vide supra*). The calculated strain energies are given in Table I. It is clear that the uns-cis isomer (Figure 2b) is lower in strain energy than the remaining four isomers. The strain about the pyridine nitrogen atoms, as described above, is comparable for all isomers. The remaining energy terms of significance are found in the aliphatic propanediamine ring. There are no significant bond length distortions or nonbonded interactions for any of these complexes.

The torsional strain energy of the propylenediamine ring calculated from our model (energy minimum for the staggered configuration) is 1.94 kcal/mol for uns-cis isomer a (Figure 2), 2.24 kcal/mol for isomer b, 3.50 kcal/mol for isomer d, and 2.60 kcal/mol for isomer e. Taken by itself, a difference of 0.36 kcal/mol in torsional strain energy is unlikely to produce stereospecific coordination. Total angle deformation strain energy for the propanediamine chelate ring is 0.71 kcal/mol for isomer a, 0.88 kcal/mol for isomer b, 2.18 kcal/mol for isomer d, and 3.33 kcal/mol for isomer e. The sum of the torsional and the angular deformation strain divides the uns-cis isomers into two groups separated by sufficiently large energy terms to generate specificity. The Λ isomers d and e appear to be sufficiently strained relative to the Δ isomers a and b to suggest that one of the latter is the observed complex, in agreement with our interpretation of

TABLE II

VAPOR-PHASE THERMODYNAMIC FUNCTIONS CALCULATED FOR SOME [Co(picpn)ox]$^+$ COMPLEXES (CAL/MOL °K)

Complex	T, °K	$-(F° - H_0°)/T$	$(H_0° - H_0°)/T$	$S°$	$C_p°$
Δ-*uns-cis*-[Co(picpn)ox]$^+$ (isomer b)	273.16	92.52	39.20	131.72	73.79
	291.16	95.09	41.47	136.56	78.13
	298.16	96.09	42.35	138.44	79.81
	303.16	96.80	42.99	139.77	81.00
	323.16	99.62	45.48	145.10	85.71
	373.16	106.60	51.64	158.23	97.05
Λ-*s-cis*-[Co(picpn)ox]$^+$ (isomer c)	273.16	95.07	40.55	135.62	74.88
	291.16	97.73	42.81	140.53	79.15
	298.16	98.75	43.68	142.43	80.80
	303.16	99.48	44.30	143.79	81.97
	323.16	102.39	46.78	149.17	86.61
	373.16	109.55	52.87	162.42	97.75

spectroscopic data. Accordingly, the Λ isomers were excluded from subsequent calculations.

The distinction between isomers a and b is not as certain. Our calculations show that isomer b lies 0.95 kcal/mol or about 10% lower in strain energy than isomer a, and that most of the energy difference is found in the cobalt valence angle deformation, in the nonbonded interactions, and in the valence angle distortions of the remainder of the picpn ligand. We tentatively assign structure b to the observed complex.

Uns-cis–S-cis Isomerization.—Though the strain energy minimization procedure does not definitively distinguish between a and b as the first formed isomer, either of these complexes may isomerize to a common s-cis isomer, c. Strain energy calculations on the s-cis isomers are summarized in Table I. Surprisingly, our calculations show that the total strain energy of the s-cis isomer c is greater than that of either uns-cis isomer a or b, with the most significant terms found in the valence-angle deformation and the torsional strain of the propanediamine chelate ring. The calculated strain energy of the s-cis isomer f is the lowest among all of the isomers, but this isomer is inaccessible *via* a simple shift of the donors of isomers a or b. Clearly, strain alone does not provide the energy for the isomerization.

We have used the thermodynamic calculation in an attempt to rationalize the experimental observations. A subroutine calculates the thermodynamic functions $(F° - H_0°)/T$, $(H° - H_0°)/T$, $S°$, and $C_p°$ at each of six temperatures supplied by the user (Table II). An ideal polyatomic gas calculation is performed using atomic coordinates, calculated in the energy minimization procedure, and the masses of the atoms to calculate the rotational contribution, and using the masses, coordinates, and force constants to calculate the vibrational contribution. Clearly, the calculations are no better than the force constants supplied as input and the coordinates calculated by the main program. The latter are also dependent on convergence of the energy minimization calculation. The result is quite approximate, and it is unlikely that the ideal gas calculations have any significance in systems which are studied as solids or as nonideal solutes.

The calculated entropy terms, Table II, show a gain of about 4 eu in the uns-cis to s-cis isomerization in the vapor phase at 25°. While the sign of the entropy change is in agreement with observation, the differences are smaller than a reasonable estimate of the effects of nonideality on the crystals or solutions. Indeed, all of the calculated energy differences are small enough to be overcome photochemically, for example. We propose that energy differences calculated within a series of isomers may be extrapolated at least to dilute solutions, if not to the solid state, and that the entropy term determines the observed uns-cis to s-cis isomerism. That the first formed isomer is not necessarily the thermodynamically stable complex corresponds to the well-documented example of nitrito–nitro isomerization among cobalt pentaammines.[8] The extremely rapid isomerization in water suggests that solvent effects are at least as great as the difference in energy between the uns-cis and s-cis isomers, though we cannot visualize a unique mechanism whereby solvent assists the molecule in attaining the thermodynamically stable configuration.

Conclusions

We have found the Boyd strain energy minimization program to be extremely useful for comparison of the strain energy within a series of stereoisomers, and we believe that a novice can use the calculation to advantage if he accepts a few constraints. The most important constraint is the willingness to carefully scrutinize the output of the program, preferrably cycle by cycle, for developments which do not coincide with intuition or experience. Literature values for the potential functions seem satisfactory; we suggest that these not be changed without substantial justification (and sufficient justification is generally beyond the ability and understanding of a novice user). A good set of potential functions will produce output which "feels right" to an experienced chemist. For example, we find that the nonbonded interactions are small for all of our isomers, with variations in the valence angle deformations frequently determining

---

(8) At the suggestion of one of the referees, we have performed the thermodynamic calculation on Δ-*uns-cis*-[Co(picpn)ox]$^+$ (isomer a (ox)). The strain energy minimization calculated converged to 13.07 kcal, or about 2.9 kcal above the strain energy calculated for the complex without inclusion of the oxalate dianion (Table I). The thermodynamic calculation produced the following results for Δ-*uns-cis*-[Co(picpn)ox]$^+$

T, °K	$-(F° - H_0°)/T$	$H_0° - H_0°/T$	$S°$	$C_p°$
273.16	94.92	41.12	136.05	76.90
291.16	97.62	43.47	141.10	81.33
298.16	98.67	44.38	143.05	83.03
303.16	99.41	45.03	144.44	84.24
323.16	102.37	47.60	149.97	89.02
373.16	109.66	53.93	163.59	100.49

from which it is seen that isomer a(ox) is more similar to isomer c(ox) than to isomer b(ox); indeed, from the calculated strain energies and thermodynamic functions, there is no apparent rationale for the observed isomerization.

the final coordinates. This result is in agreement with a force field which includes a relatively large number of nonbonded interactions. At the potential energy minimum of the nonbonded interactions, the relatively fewer valence angles are deformed to strike a net potential energy balance. We interpret the lack of any single dominant strain energy term to indicate that the initial model is reasonably correct.

We have also found that the initial coordinate set may be easily obtained from molecular models, and that this set does not lead to any unusual problems of convergence or false minima. To our knowledge, we have encountered a false minimum only once, and then as a result of an improperly specified interaction set. The false minimum was immediately obvious from an examination of a molecular model—the methyl group appeared as a trigonal plane. We cannot place enough emphasis on the importance of careful and continuous interaction between the computer and the user.

For the present, we doubt that it is possible to specify a force field which will permit exact calculation of the strain energies of a molecule. Moreover, it is highly unlikely that strain energies will ever be determined experimentally.[9] We do believe, however, that comparison of the strain energy within a series of isomers is valid *if* the same potential functions and the same number and kind of interactions are used, and the same degree of convergence is achieved in each calculation. We hope that under these conditions, differences of the order of 10% are meaningful.

Acknowledgments.—The authors gratefully acknowledge a grant of computer time from the graduate school of the Illinois Institute of Technology, helpful discussions with Daryle Busch, Louis De Hayes, and Ken Raymond, and a copy of a listing and writeup for the program MOLBD supplied by R. H. Boyd.

---

(9) Among the few examples of experimentally determined conformational energies the classical equilibrium study of Dwyer and coworkers (*J. Amer. Chem. Soc.*, **85**, 2913 (1963)) remains unique. Most recently, the pmr probe has come into extensive use; a recent paper by Sudmier and Blackmer (*Inorg. Chem.*, **10**, 2010 (1971)) includes a thorough bibliography of recent applications, as well as an elegant example.

CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY,
WAYNE STATE UNIVERSITY, DETROIT, MICHIGAN 48202

Outer-Sphere Reductions of Cobalt(III) Complexes Containing Macrocyclic Ligands. A Further Examination of Free Energy Correlations and Anomalous Reorganizational Barriers[1]

BY D. PAUL RILLEMA AND JOHN F. ENDICOTT*

Received January 24, 1972

The outer-sphere reductions of several *trans*-$Co(N_4)(NH_3)_2^{3+}$ complexes have been examined, with Cr^{2+}, V^{2+}, and $Ru(NH_3)_6^{2+}$ as reducing agents and N_4 as a tetradentate macrocyclic ligand. For any reducing agent, the rate constants for the reductions are not very different; however when corrections are made for variations in the reduction potentials of the cobalt(III) complexes, the rate constant increases by about 10^2 when N_4 is changed from a tetraamine to a tetraimine. This variation in reactivity does not agree with current theories of electron-transfer rates and the known variation of Co(III)–Co(II) self-exchange rates. The discrepancy can be attributed to anomalous variations in the Marcus reorganizational parameter (λ). It appears that in reductions of cobalt(III), the reorganizational parameters depend more strongly on the reducing agent and more weakly on cobalt(III) than predicted.

Introduction

Linck[2] has recently articulated the two somewhat antagonistic approaches frequently used in analyses of the reactivity patterns observed in the electron-transfer reactions of transition metal complexes. Thus one frequently encounters attempts to rationalize reactivity patterns in terms of "electronic–structural" relationships, which take no specific account of distinctions between intrinsic ligand reorganizational barriers and the contributions of the free energy of reaction (see ref 2 for a sympathetic representation of this approach and for appropriate documentation). The contrasting approach, which attempts to analyze reactivity patterns in terms of intrinsic reorganizational barriers, taking account of any contributions due only to free energy of reaction, has been most successfully organized in terms of a free energy correlation such as that proposed by Marcus.[3–6]

$$\Delta G_{12}^{\ddagger} = \frac{\lambda_{12}}{4} + \frac{\Delta G_{12}^{\circ}}{2} + \frac{(\Delta G_{12}^{\circ})^2}{4\lambda_{12}} \qquad (1)$$

Until very recently attempts to apply eq 1 to the much studied reactions of cobalt(III) have been frustrated because there have been few reliable estimates of the thermodynamic parameters. This has led to some

---

(1) (a) Partial support of this research by the Public Health Service (Grant AM 14341) is gratefully acknowledged. (b) Presented in part at the 163rd National Meeting of the American Chemical Society, Boston, Mass., April 1971.

(2) R. G. Linck, *MTP Int. Rev. Sci., Inorg. Chem.*, [1] **9**, 303 (1972).

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

(4) W. L. Reynolds and R. W. Lumry, "Mechanisms of Electron Transfer," Ronald Press, New York, N. Y., 1966.

(5) (a) R. A. Marcus, *J. Phys. Chem.*, **67**, 853 (1963); (b) *ibid.*, **72**, 891 (1968).

(6) In eq 1, $\Delta G_{12}^{\ddagger}$ is the overall free energy of activation, λ_{12} is the intrinsic reorganizational parameter, and ΔG_{12}° is the overall free energy of reaction. Subscripts refer to reaction of oxidant 1 with reductant 2. In the specific discussion of cobalt reactions it will be convenient to use λ_{Co} and and λ_{Red} (rather than λ_{11} and λ_{22}, respectively) for the reorganizational parameters observed in self-exchange reactions.