the rich chemistry of α-chloro nitrones have resulted in the discovery of numerous synthetically significant transformations.[72]

Conclusion

We have attempted to show the development of a general methodology applicable to the synthesis of a variety of alkaloidal classes (e.g., the pyrrolizidine, quinolizidine, indolizidine, lycopodium, and tropane classes). The cycloadditions discussed are normally well-behaved,[73] efficient reactions. The inherent features of carbon–carbon bond formation, oxygen transfer, and nitrogen incorporation have been joined by the high site selectivities, regioselectivities, and stereoselectivities often observed in nitrone–alkene cycloadditions to render these reactions powerful weapons in the arsenal of the organic chemist. Indeed, it is our firm conviction that such processes will play an ever increasing role in the expansionary phase that is currently underway in organic synthesis.

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Role of Activation Volume in the Elucidation of Reaction Mechanisms in Octahedral Coordination Complexes

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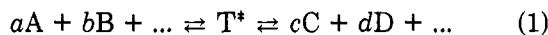*Department of Inorganic Chemistry, University of Melbourne, Parkville 3052, Australia*

The effect of pressure on the rate of a chemical reaction in solution, which can be attributed to a volume change occurring in the activation step, has been gaining recognition as an aid in mechanistic elucidation. The existence of a correlation between the main mechanistic features of a reaction and the activation volume is now widely accepted. Extensive studies of organic reactions using this technique have appeared.[2] However, applications of the effect of pressure in the area of inorganic reaction mechanisms are still limited, though growing steadily.

Advances in modern high-pressure techniques and equipment have made the measurement of the effect of pressure on reaction rate relatively simple. Activation enthalpies and entropies obtained from the effect of temperature on reaction rates can now be supplemented by activation volumes obtained from the pressure dependence of reaction rates. The interpretation of mechanism based on entropy change requires a structural concept involving inferred changes in both energy and nuclear position; volume change is based on changes in nuclear position only, and should therefore be inherently simpler to intercept.

The *activation volume* ($\Delta\bar{V}^*$) for the generalized reaction

$$aA + bB + \ldots \rightleftarrows T^* \rightleftarrows cC + dD + \ldots \quad (1)$$

can be defined as[3]

$$\Delta\bar{V}^* = -RT(\partial \ln k_\mathrm{p}/\partial P)_T \quad (2)$$

which can also be written in terms of partial molar volumes ($\bar{V}_i$) as

$$\Delta\bar{V}^* = \bar{V}_{T*} - a\bar{V}_A - b\bar{V}_B - \ldots = \bar{V}_{T*} - \sum_A a\bar{V}_A \quad (3)$$

The *reaction volume* ($\Delta\bar{V}^\circ$), or partial molar volume change for the reaction, can be expressed as

$$\Delta\bar{V}^\circ = -RT(\partial \ln K/\partial P)_T \quad (4)$$

or

$$\Delta\bar{V}^\circ = (c\bar{V}_C + d\bar{V}_D + \ldots) - (a\bar{V}_A + b\bar{V}_B + \ldots) \quad (5)$$

$$= \sum \bar{V}_\mathrm{products} - \sum \bar{V}_\mathrm{reactants} \quad (6)$$

For convenience, it has become common practice to delete the bar over the volume symbol used to indicate partiality and, subsequently, *activation volume* will be symbolized by ΔV^* and *reaction volume* by ΔV°. The activation volume can be calculated only from the effect of pressure on the rate constant and application of eq 2. The reaction volume can be determined by dilato-

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metry, by measuring the effect of pressure on the equilibrium constant K, or by combination of separately determined partial molar volumes of all reactants and products in eq 6.

The exact theoretical relationship between rate and pressure and equilibrium constant and pressure is not known; hence the calculation of $\Delta V^{\ddagger}$ must be empirical in nature. Frequently, but not always, $\Delta V^{\ddagger}$ itself shows a pressure dependence; the slopes of $\ln k_P$ vs. P graphs then decrease with increasing pressure. The most popular empirical equation is a quadratic of the form[4]

$$\ln k_P = \ln k_0 + bP + cP^2 \qquad (7)$$

Despite the fact that the shape is not realistic (it demands an extremum) at very high pressures, eq 7 accurately describes a variety of reactions at the moderate pressures employed in most experiments. From eq 7, the activation volume at any pressure is given as

$$\Delta V^{\ddagger}{}_P = -bRT - 2RTcP \qquad (8)$$

and the generally quoted volume of activation at zero pressure is

$$\Delta V^{\ddagger} = -bRT \qquad (9)$$

$\Delta V^{\ddagger}$ is positive when the rate decreases upon the application of pressure and negative when the rate increases with increased hydrostatic pressure. It is frequently possible to determine $\Delta V^{\ddagger}$ with uncertainties of less than $\pm 1 \mathrm{cm}^3\,\mathrm{mol}^{-1}$, and it is now clear that $\Delta V^{\ddagger}$ is usually determined more reliably than $\Delta S^{\ddagger}$.

The pressure dependence of the activation volume, from the curvature in the $\ln k_P$ vs. P graph, can be represented by a term called the *compressibility coefficient of activation* ($\Delta \beta^{\ddagger}$), defined by eq 10. We can

$$\Delta \beta^{\ddagger} = -(\partial \Delta V^{\ddagger}/\partial P)_T = 2RTc \qquad (10)$$

also express $\Delta \beta^{\ddagger}$ in terms of the difference in compressibility coefficients (β) of the transition state and all reactants as

$$\Delta \beta^{\ddagger} = (-\partial V^{\ddagger}/\partial P)_T - \sum_A a(\partial V_A/\partial P)_T \qquad (11)$$

$$= \beta^{\ddagger} - \sum_A a\beta_A \qquad (12)$$

A further term sometimes employed is the similar-sounding *compressibility of activation* ($\Delta \kappa^{\ddagger}$), simply defined as

$$\Delta \kappa^{\ddagger} = \Delta \beta^{\ddagger}/\Delta V^{\ddagger} \qquad (13)$$

It is convenient for a simplified analysis of activation volumes to consider octahedral coordination complex ions as essentially incompressible spherical species with a characteristic average radius.[5,6] It has been assumed that a five-coordinate intermediate (ML_5) arising from dissociative release of a neutral ligand (L) will occupy the same volume as its six-coordinate precursor (ML_6).[5] The volume of $Ni(NH_3)_6{}^{2+}$ (138 $cm^3\,mol^{-1}$) is identical with that calculated for the hypothetical $Ni(NH_3)_5{}^{2+}$ cation.[5] For the analogous cobalt(III) system, the intermediate $Co(NH_3)_5{}^{3+}$ has been recently estimated[7] to have the same volume as $Co(NH_3)_6{}^{3+}$ ($\bar V$ = 55 cm^3

Table I
Partial Molar Volume and Compressibility Coefficient of
Water in Bulk and Electrostricted Environments[a]

environment	V, $cm^3\,mol^{-1}$	β, $cm^3\,mol^{-1}\,kbar^{-1}$
bulk solvent	18.0	0.84
second hydration layer	15.6	0.22
first hydration layer	15.0	0.12
coordination sphere	$14 \to 15$	$0.06 \to 0.12$

[a] Estimated for a 3+ ion.

mol^{-1}). For an associative mechanism, the seven-coordinate intermediate (ML_7) formed by incorporation of a ligand may likewise occupy approximately the same intrinsic volume as its precursor ML_6. Subsequently, for neutral ligands L, the dissociative mechanism is expected to lead to a transition state (ML_5 + L) of greater volume than the ML_6 precursor (positive $\Delta V^{\ddagger}$); the associative mechanism should produce a transition state (ML_7) of less volume than the combined volumes of ML_6 and L (negative $\Delta V^{\ddagger}$).

Since we are dealing generally with the reactions of ionic species in solution, it is most important to appreciate that the partial molar volume of a complex ion involves two major components. The first is the intrinsic volume (V_{intr}) arising, in the case of complex cations, from the bulk of groups within the coordination sphere. However, the electrostatic interaction of the charged ion with the solvent (V_{el}) is also significant. An ion introduced into a solvent causes a significant contraction of the system; this is termed *electrostriction* of the solvent. Since the entering or leaving groups are commonly charged, the electrostrictive effect should not be neglected. In terms of the activated state, we may, therefore, partition $\Delta V^{\ddagger}$ into *intrinsic* and *electrostrictive* components. The latter effect may frequently be the dominant contributor to the experimentally determined activation volume. A consequence of electrostriction is the formation of ordered layers of solvent molecules, or solvation spheres, about a charged complex ion. Both the partial molar volume and compressibility coefficient of the solvent vary on transition from "bulk" solvent to solvation sphere or coordination sphere.[5,8] The relevant variation for water is shown in Table I. Subsequently, reactions of ionic complexes which exhibit a marked pressure dependence of $\Delta V^{\ddagger}$ itself (i.e., $\Delta \beta^{\ddagger} \neq 0$) commonly exhibit dominant electrostrictive contributions to $\Delta V^{\ddagger}$.

The preceding discussion has generally been based on octahedral metal ions. It is in these complexes that we have been principally interested, and this Account is restricted to a discussion of complexes of this type. Further, the relative insensitivity of most physical properties of water to applied pressure[9] and its prominence in solution kinetics make it an excellent choice of solvent for our purposes; most of the systems discussed will involve aqueous solutions. The type of reactions which we have been investigating can be followed conveniently by the use of apparatus pressurized routinely to at least 1720 bar (25 000 psi). This pressure range is sufficient to determine $\Delta V^{\ddagger}$ with acceptable accuracy for most reactions. One technique employs a sampling vessel fitted with a high-pressure tap which

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allows aliquots to be withdrawn at appropriate intervals. These aliquots are then immediately subjected to some physical measurement to ascertain the reaction rate. We have employed this technique in studies of racemization reactions. The alternative method is to follow the rate of reaction spectrophotometrically in situ using a high-pressure spectrophotometer cell with sapphire windows.[10]

Experimental Applications

Racemization Reactions. Prior to 1977, no activation volumes had been reported for racemization reactions of octahedral complexes in solution, despite the continuing interest in these systems in the chemical literature. Subsequent to our first report,[11] several other studies have appeared.[12-14]

Both intermolecular and intramolecular mechanisms have been proposed for racemization in octahedral chelate complexes.[15] The intermolecular mechanism (eq 14), involving complete loss of one chelate, has been

$$\text{(14)}$$
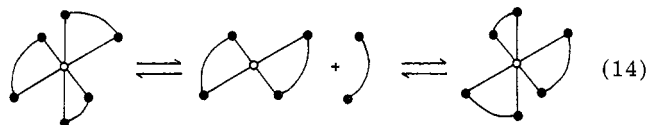
characterized by isotopic exchange studies for Ni(phen)$_3^{2+}$, a suitable example of this type of mechanism.[16]

Two different types of intramolecular mechanisms can be considered for complexes with bidentate ligands and are differentiated by whether racemization occurs with or without bond rupture.[15] A one-ended dissociation (eq 15) involves bond breaking of one chelate bond

$$\text{(15)}$$

$$\text{(16)}$$
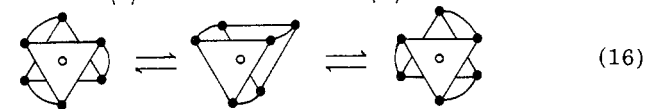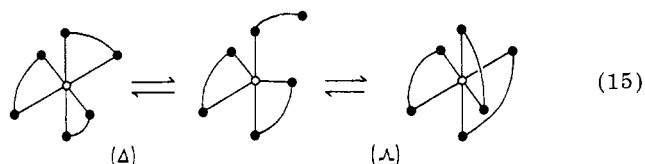
accompanied by rearrangement to a five-coordinate transition state. Alternatively a twist mechanism (eq 16) proceeding without bond rupture by way of an inactive trigonal prismatic transition state can be considered.

Although the partial molar volume of each optical isomer will be identical (i.e., $\Delta V^0 = 0$), the partial molar volume of the transition state need not be the same as that of the precursor. If we assume that the five-coordinate intermediate volume is changed only because of

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Table II
Activation Volumes and Entropies for Selected Racemization and Geometrical Isomerization Reactions of Octahedral Complexes[a]

complex	$\Delta V^{\ddagger}$, cm^3 mol^{-1}	$\Delta S^{\ddagger}$, J K^{-1} mol^{-1}	ref
Racemization			
Cr(ox)$_3^{3-}$	-16.3 ± 0.4	-76 ± 8	11
Cr(ox)$_2$(phen)$^-$	-12.3 ± 0.3	-69 ± 7	11
Cr(ox)$_2$(bpy)$^-$	-12.0 ± 0.3	-79 ± 9	11
Cr(ox)(phen)$_2^+$	-1.5 ± 0.3	-64 ± 6	11
Cr(ox)(bpy)$_2^+$	-1.0 ± 0.2	-69 ± 4	11
Cr(phen)$_3^{3+}$	$+3.3 \pm 0.3$	-56 ± 8	11
Cr(bpy)$_3^{3+}$	$+3.0 \pm 0.3$	-63 ± 8	11
Fe(phen)$_3^{2+}$	$+15.6 \pm 0.3$	$+89 \pm 8$	12
Ni(phen)$_3^{2+}$	-1.5 ± 0.3	$+12 \pm 3$	12
Ni(phen)$_2$(bpy)$^{2+}$	-0.1 ± 0.1	$+7 \pm 20$	13
Ni(phen)(bpy)$_2^{2+}$	-5.2 ± 0.5^b	$+16 \pm 12$	13
	-1.9 ± 0.2^c	$+13 \pm 12$	13
Co(pdtc)$_3$	$+9.8 \pm 0.4^d$	$+18 \pm 12$	14
	$+7.8 \pm 0.4^e$	$+51 \pm 25$	14
	$+5.2 \pm 0.3^f$	$+35 \pm 10$	14
	$+5.4 \pm 0.3^g$	$+11 \pm 12$	14
Isomerization			
trans-Cr(ox)$_2$(OH$_2$)$_2^-$	-16.6 ± 0.5 $(-1.8)^h$	-61 ± 5	21
trans-Cr(mal)$_2$(OH$_2$)$_2^-$	$+8.9 \pm 0.3$	$+74 \pm 5$	21
trans-Co(en)$_2$-(SeO$_3$H)(OH$_2$)$^{2+}$	$+7.5 \pm 0.2$	$+53 \pm 4$	5, 20
trans-Co(en)$_2$(OH$_2$)$_2^{3+}$	$+14.3 \pm 0.2$ $(+1.0)^h$	$+103 \pm 5$	19
trans-Co(en)$_2$-(CH$_3$COO)(OH$_2$)$^{2+}$	$+7.9 \pm 0.3$	$+61 \pm 9$	22
trans-Co(en)$_2$-(SeO$_3$)(OH$_2$)$^+$	$+7.3 \pm 0.2$	$+36 \pm 7$	5, 20
trans-Co(en)$_2$-(OH)(OH$_2$)$^{2+}$	$+14.5 \pm 1.1$	$+100 \pm 20$	20

[a] Determined in dilute aqueous acid except where indicated. [b] 1.0 M acid. [c] 0.01 M acid. [d] Ethanol. [e] Toluene. [f] Dimethylformamide. [g] Acetonitrile. [h] Nonzero $\Delta\beta^{\ddagger}$, cm^3 mol^{-1} kbar^{-1}, in parentheses.

motion of the leaving group out of the first coordination sphere, the one-ended dissociative mechanism in the case of a neutral ligand should lead to a transition state of greater volume than its precursor due to this extension of the dangling arm into the solvent. Hence a positive $\Delta V^{\ddagger}$ is predicted. When the dissociated arm is charged, however, solvent electrostriction of the new charge center will dominate, causing an effective decrease in volume; hence a negative $\Delta V^{\ddagger}$ is then expected. To a first approximation, since a twist mechanism in the absence of any spin-change preequilibrium can be assumed to occur without bond extension and only with bond angle distortions, no change in volume in the transition state is predicted, and hence $\Delta V^{\ddagger}$ should be zero.

The first study of intramolecular racemization at elevated pressures, that of the chromium(III) complexes Cr(aa)$_{3-n}$(ox)$_n^{(3-2n)+}$ (aa = 2,2'-bipyridyl (bpy or 1,10-phenanthroline (phen); ox^{2-} = oxalate; $n = 1 \rightarrow 3$), produced a clear mechanistic differentiation.[11] Large negative $\Delta V^{\ddagger}$ values for Cr(ox)$_3^{3-}$ and Cr(ox)(aa)$_2^-$ contrasted with near-zero $\Delta V^{\ddagger}$ for the remaining reactions (Table II). These disparate $\Delta V^{\ddagger}$ have been interpreted in terms of a one-ended dissociative mechanism with a dangling ligand for the former complexes and a twist mechanism for others.

A great deal of evidence has established a dissociative intermolecular mechanism for racemization of Ni(phen)$_3^{2+}$ (eq 14).[16] The $\Delta V^{\ddagger}$ for racemization[12] is -1.5

$cm^3 mol^{-1}$, which cannot be readily reconciled with an intermolecular mechanism. However, $\Delta V^{\ddagger}$ for racemization and aquation are identical, as expected, and arguments relating to solvation effects or bond length changes of coordinated ligands in the transition state have been presented to account for the small $\Delta V^{\ddagger}$. The mixed-ligand complexes $Ni(phen)_2(bpy)^{2+}$ and $Ni(phen)(bpy)_2^{2+}$ also show small $\Delta V^{\ddagger}$ (Table II).[13] While the rigid phen ligand cannot participate in a one-ended dissociation for steric reasons, the bpy ligand can twist about the $C(2)-C(2')$ bond linking the pyridine rings. The acid dependence of $\Delta V^{\ddagger}$ observed, particularly with $Ni(phen)(bpy)_2^{2+}$, is consistent with the favored mechanism, where protonation of the one-ended dissociated bpy ligand can occur. A similar acid dependence of $\Delta V^{\ddagger}$ is observed for aquation of $Fe(bpy)_3^{2+}$, where an analogous mechanism is favored. Small $\Delta V^{\ddagger}$ observed for the nickel complexes are consistent with the expectation of the chelated and partly dissociated bpy ligands sweeping out similar volumes.

Interpretation of $\Delta V^{\ddagger}$ for racemization of $Fe(phen)_3^{2+}$ is complicated by a significant positive contribution, estimated as approximately 9 $cm^3 mol^{-1}$, from a preequilibrium excitation from the low-spin ground state to a high-spin state with concomitant general metal–ligand bond lengthening.[12] The moderately small residual component of $\Delta V^{\ddagger}$ could be consistent with the previously proposed twist mechanism.

Some preliminary studies of the pressure dependence of racemization of neutral tris(dithio-carbamato)cobalt(III)complexes in a range of nonaqueous solvents have been completed.[14] The positive $\Delta V^{\ddagger}$ values determined with the pyrrolidine chelate (pdtc) in several solvents (Table II) are not consistent with either a one-ended dissociative mechanism for a negatively charged ligand or with a simple twist mechanism. However, a spin preequilibrium prior to a twist process, such as that proposed for racemization of $Fe(phen)_3^{2+}$, would account for the positive $\Delta V^{\ddagger}$. The observation that $\Delta V^{\ddagger}$ and $\Delta \kappa^{\ddagger}$ are not appreciably solvent dependent supports a twist mechanism, as does NMR evidence for a related system.[17] It is possible that twisting motions may be more facile in the proposed "expanded" high-spin transition state. Such a spin preequilibrium can be expected to make substantial positive contributions to both $\Delta V^{\ddagger}$ and $\Delta S^{\ddagger}$.

Geometrical Isomerization Reactions. The first activation volumes for geometrical isomerization of octahedral complexes were reported in 1972,[18] and accelerated interest in this area has subsequently led to a number of similar studies[5,19-24] (Table II). Mechanisms that can lead to geometrical isomerization are analogous to those that may lead to racemization.[15] For complexes of the type $M(aa)_2L_2^{n+}$ (aa = bidentate ligand), dissociative, twist, or associative mechanisms can be considered. One-ended dissociation of a bidentate ligand (eq 17), dissociation of a unidentate ligand (eq 18), twisting

$$(17)$$

$$(18)$$

$$(19)$$

$$(20)$$
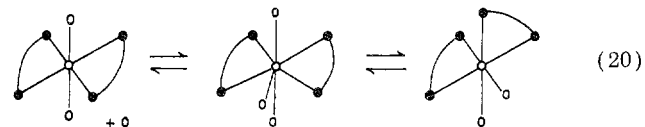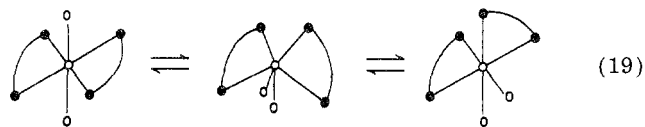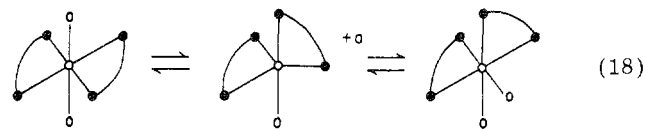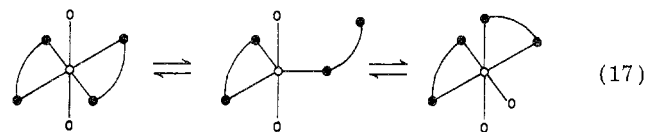
(eq 19), or an associative mechanism (eq 20) can lead to isomerization. Unlike racemization reactions the partial molar volumes of the geometric isomers need not be the same, and both ΔV^0 and $\Delta V^{\ddagger}$ may be nonzero.

Predicted $\Delta V^{\ddagger}$ generally follow arguments developed in the earlier section. In the case of dissociative aquo ligand release, complete release into the first solvation sphere would involve in the upper limit a positive contribution due to the intrinsic volume of water in that environment of +15 $cm^3 mol^{-1}$. This analysis assumes that the five-coordinate intermediate retains the same volume as its precursor, and that solvation of the ionic precursor and transition states are similar for a neutral leaving group. The arguments for an associative mechanism are the reverse of the above, leading to a predicted upper limit to $\Delta V^{\ddagger}$ of −15 $cm^3 mol^{-1}$.

The success of $\Delta V^{\ddagger}$ in the elucidation of mechanisms of geometrical isomerization is exemplified by a study of *trans-* → *cis-*$Cr(aa)_2(OH_2)_2$ for aa^{2-} = oxalate ($\Delta V^{\ddagger}$ = −16.6 $cm^3 mol^{-1}$) and aa^{2-} = malonate ($\Delta V^{\ddagger}$ = +8.9 $cm^3 mol^{-1}$).[21] $\Delta V^{\ddagger}$ for the former complex is consistent with the established mechanism of one-ended dissociation of a chelated oxalate and similar to $\Delta V^{\ddagger}$ for racemization of $Cr(ox)_3^{3-}$ which proceeds via the same mechanism.[11] The markedly different $\Delta V^{\ddagger}$ for the malonate complex provides definitive evidence for a different mechanism, and release of an aquo ligand in the transition state (eq 20) is favored in this case.

Studies of a series of reactions of the type *trans-* → *cis-*$Co(en)_2(OH_2)(X)^{n+}$ (en = 1,2-diaminoethane; X = OH_2, SeO_3H^-, SeO_3^{2-}, CH_3COO^-) have provided positive $\Delta V^{\ddagger}$ values in each case, consistent with a general dissociative mechanism of aquo ligand release.[5,22] Variation in the size of $\Delta V^{\ddagger}$ and $\Delta \beta^{\ddagger}$ (Table II) may indicate minor mechanistic differentiation. Complete dissociative release of a water molecule from the coordination sphere to the bulk solvent (characterized as a D mechanism) should lead to larger $\Delta V^{\ddagger}$ and $\Delta \beta^{\ddagger}$ than for water interchange between the coordination and first solvation spheres (an I_d mechanism). There are some grounds for assigning a D mechanism for the X = OH_2 complex and an I_d mechanism for the others on the basis of this analysis,[22] although the extraction of such detail from

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complex	$\Delta V^{\ddagger}$, cm^3 mol^{-1}	$\Delta\beta^{\ddagger}$, cm^3 mol^{-1} kbar^{-1}	ΔV°, cm^3 mol^{-1}	ref
Aquation: Unidentate Ligands[a]				
$Co(NH_3)_5(Cl)^{2+}$	-10.6 ± 0.4	-2.1 ± 0.2	-11.6	29
$Co(NH_3)_5(Br)^{2+}$	-9.2 ± 0.2	-2.0 ± 0.2	-10.8	29
$Co(NH_3)_5(SO_4)^{+}$	-18.5 ± 0.7	-4 ± 0.5	-19.2	29
$Co(NH_3)_5(OH_2)^{3+}$	$+1.2 \pm 0.1$	0	0.0	30
$Cr(NH_3)_5(OH_2)^{3+}$	-5.8 ± 0.2	0	0.0	31
$Cr(NH_3)_5(Cl)^{2+}$	-10.8 ± 0.3	-1.0 ± 0.2	-8.4	28
$Cr(NH_3)_5(Br)^{2+}$	-10.2 ± 0.3	-1.0 ± 0.1	-8.4	28
$Co(NH_3)_5(Me_2SO)^{3+}$	-1.7 ± 0.7	0		7
$Co(NH_3)_5(urea)^{3+}$	$+1.3 \pm 0.5$	0		35
$Co(dmg)_2Cl(urea)$	$+3.5 \pm 0.3$	0		34
$trans$-Co(dtcd)-(N$_3$)Cl$^+$	$+8.7 \pm 0.4$	0		36
Aquation: Bidentate Ligands[b]				
$trans$-Cr(ox)$_2$-(OH$_2$)$_2^-$	$+1.7 \pm 0.7$	0		21
$trans$-Cr(mal)$_2$-(OH$_2$)$_2^-$	$+2.4 \pm 0.6$	0		21
$Fe(phen)_3^{2+}$	$+15.4 \pm 0.3$	0		37
$Fe(bpy)_3^{2+}$	$+11.5 \pm 0.7$	0		24
$Ni(phen)_3^{2+}$	-1.2 ± 0.2	0		12
Base Hydrolysis				
$Co(NH_3)_5Br^{2+}$	$+8.5$	$-$		38
$Co(NH_3)_5(SO_4)^{+}$	$+19.5 \pm 1.1$	$+9.5 \pm 2.2$		5
$Co(NH_3)_5(PO_4)$	$+28.9 \pm 2.2$	$+7.7 \pm 2.1$		5
$Co(NH_3)_5(ONO)^{2+c}$	$+27.0 \pm 1.4$	$+4 \pm 2$		40

[a] Dilute aqueous acid. [b] $\geqslant 1.0$ M aqueous acid. [c] Base-catalyzed linkage isomerization.

activation volume data at present should be treated with some reserve.

Examination of data in Table II indicates that there is a correlation between $\Delta V^{\ddagger}$ and $\Delta S^{\ddagger}$ in most cases. Such an expected relationship has been reported previously,[25] most recently for aquation reactions of inert complexes.[26] Since positional changes in the transition state contribute to both $\Delta V^{\ddagger}$ and $\Delta S^{\ddagger}$ in the same sense, a correlation is likely; however, an exact relationship is not necessary as rotational contributions to $\Delta S^{\ddagger}$, for example, need not contribute to $\Delta V^{\ddagger}$. An analysis of the available data for racemization and geometrical isomerization of octahedral complexes in solution[27] indicates that a fairly good linear relationship is obtained except for the racemization of $Cr(aa)_3^{3+}$ and $Cr(aa)_2$-(ox)$^+$ (aa = phen or bpy) which are predicted to involve a simple trigonal twist mechanism; this twist mechanism is expected to lead to a negative $\Delta S^{\ddagger}$ and a zero $\Delta V^{\ddagger}$. Least-squares analysis of all available data predicts a small positive $\Delta S^{\ddagger}$ for a near-zero $\Delta V^{\ddagger}$. This is observed in the racemization of $Ni(phen)_3^{2+}$, in which case there is firm evidence for a dissociative intermolecular mechanism rather than a twist mechanism. Absence of a correlation of $\Delta V^{\ddagger}$ and $\Delta S^{\ddagger}$ for racemization and isomerization may, therefore, be indicative of a twist mechanism.

Hydrolysis Reactions. Two of the first systematic studies of activation volumes for metal complexes reported aquation reactions of series of $Co(NH_3)_5X^{n+}$ and of $Cr(NH_3)_5X^{n+}$ complexes (Table III).[28,29] Determined

$\Delta V^{\ddagger}$ and ΔV^0 were interpreted in terms of dissociative and associative character, respectively. The value of using ΔV^0 in conjunction with $\Delta V^{\ddagger}$ for mechanistic elucidation in these systems has recently been clearly presented by Kelm.[7] The contrast between the dissociative reactions of cobalt(III) and the apparently associative reactions of chromium(III) is most conveniently illustrated by $\Delta V^{\ddagger}$ for solvent exchange in the aquo complexes,[30,31] with $\Delta V^{\ddagger} = +1.2$ cm^3 mol^{-1} for $Co(NH_3)_5(OH_2)^{3+}$ but $\Delta V^{\ddagger} = -5.8$ cm^3 mol^{-1} for $Cr(NH_3)_5(OH_2)^{3+}$. Aquo exchange in cis-Co(en)$_2$(OH$_2$)$_2^{3+}$ similarly proceeds[32] with $\Delta V^{\ddagger} = +5.9$ cm^3 mol^{-1}, while a $\Delta V^{\ddagger} = -9.3$ cm^3 mol^{-1} has been reported[33] for exchange in $Cr(OH_2)_6^{3+}$. Since release of a neutral ligand can be anticipated to produce very small volume changes of an electrostrictive nature,[5] a positive $\Delta V^{\ddagger}$ is diagnostic of a dissociative mechanism and a negative $\Delta V^{\ddagger}$ diagnostic of an associative mechanism above.

The situation in reactions where release or displacement of a charged ligand occurs in the transition state is complicated by significant electrostrictive contribution to $\Delta V^{\ddagger}$ in addition to intrinsic volume changes. This can be seen from comparison of $\Delta V^{\ddagger}$ for aquation of $Co(NH_3)_5(SO_4)^{+}$, $Co(NH_3)_5Cl^{2+}$, and $Co(NH_3)_5$-(Me$_2$SO)$^{3+}$, for which values of -18.5, -10.6 and -1.7 cm^3 mol^{-1}, respectively, are obtained as the charge on the leaving group varies from $2-$ to $1-$ to 0.

The role of the nonleaving groups in determining the size and sign of $\Delta V^{\ddagger}$ has not yet been subjected to extensive investigation. Aquation of the formally neutral complex $Co(dmg)_2(urea)Cl$ (dmg = dimethylglyoximato$^-$) occurs with loss of O-bound urea. A $\Delta V^{\ddagger}$ of $+3.5$ cm^3 mol^{-1} is consistent with a dissociative mechanism, the small size suggesting an interchange (I$_d$) mechanism.[34] A $\Delta V^{\ddagger}$ of $+1.3$ cm^3 mol^{-1} has been observed for aquation of urea in the $Co(NH_3)_5(urea)^{3+}$ cation. The similarity of $\Delta V^{\ddagger}$ in the two complexes of different charge but identical neutral leaving group is consistent with minor contributions only from change in solvation of the ground and transition states.[35] $\Delta V^{\ddagger}$ for chloride aquation in $trans$-Co(dtcd)(N$_3$)Cl$^+$ (dtcd = 5,12-dimethyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene) is[36] $+8.7$ cm^3 mol^{-1}, in contrast to a $\Delta V^{\ddagger}$ of -10.6 cm^3 mol^{-1} for aquation of $Co(NH_3)_5Cl^{2+}$. This positive $\Delta V^{\ddagger}$ is certainly consistent with the accepted dissociative mechanism. However, the significant variation from the value for $Co(NH_3)_5Cl^{2+}$ suggests that the large, bulky macrocycle may determine that electrostrictive solvation of chloride ion is less marked in that complex than in the pentaammine complex, even when substantial bond stretching has occurred.

Hydrolysis reactions involving release of bidentate rather than unidentate ligands (Table III) are often complicated by the possibility of several stepwise pathways for hydrolysis which nevertheless yield a similar

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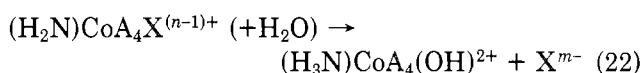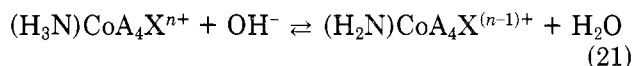(26) M. V. Twigg, Inorg. Chim. Acta, 24, L84 (1977).
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$\Delta V^{\ddagger}$. Some mechanistic information can still be forthcoming. For example, the essentially identical $\Delta V^{\ddagger}$ for acid-catalyzed aquations of $Co(ox)_2(OH_2)_2^-$ (+1.7 cm^3 mol^{-1}) and $Cr(mal)_2(OH_2)_2^-$ (+2.4 cm^3 mol^{-1}) are consistent with one mechanism operating for both aquation reactions, in contrast to the different mechanisms established for geometrical isomerization of these complexes from $\Delta V^{\ddagger}$ data.[21] Aquation of $Fe(phen)_3^{2+}$ and $Fe(bpy)_3^{2+}$ both show large positive $\Delta V^{\ddagger}$, consistent with dissociative release of a neutral chelate.[12,24,37]

Some activation volumes have been reported for base hydrolysis reactions (Table III).[5,38] In terms of the favored conjugate base mechanism for base hydrolysis, one may write

$$(H_3N)CoA_4X^{n+} + OH^- \rightleftarrows (H_2N)CoA_4X^{(n-1)+} + H_2O \tag{21}$$

$$(H_2N)CoA_4X^{(n-1)+} (+H_2O) \rightarrow (H_3N)CoA_4(OH)^{2+} + X^{m-} \tag{22}$$

Contributions from both charge neutralization of hydroxide ion on formation of the conjugate base (eq 21, ΔV_{CB}) and from further intrinsic and electrostatic volume changes on release of X^{m-} (eq 22, $\Delta V^{\ddagger}_X$) are expected. Despite the change in overall charge on the complex ion on forming the conjugate base, the ΔV_{CB} contribution may approach the volume of electrostriction for OH$^-$ (+22 cm^3 mol^{-1})[39] since ions such as $Co(NH_3)_5(OH_2)^{3+}$ and $Co(NH_3)_5(OH)^{2+}$ have similar partial molar volumes.[5] The generally positive $\Delta V^{\ddagger}$ observed to date are consistent with a large ΔV_{CB} contribution, which is only partially offset by contributions from leaving group release (Table III). A conjugate base mechanism has also been identified recently in the base-catalyzed isomerization of $Co(NH_3)_5(ONO)^{2+}$,[40] where a positive $\Delta V^{\ddagger}$ of +27 cm^3 mol^{-1} contrasts with a $\Delta V^{\ddagger}$ of -6.7 cm^3 mol^{-1} previously reported[41] for the spontaneous linkage isomerization.

The concept of a relationship between $\Delta V^{\ddagger}$ and $\Delta S^{\ddagger}$ has been introduced previously.[25-27] A correlation has already been discussed above for racemization and geometrical isomerization, and recently a linear correlation for aquation reactions of inert complexes has also been presented.[26] It should be emphasized again that an exact relationship should not be inferred, nor is it commonly observed.

Substitution Reactions. Several reactions involving substitution by ligands other than water have been studied in which $\Delta V^{\ddagger}$ have provided mechanistic information. The interchange reactions[42] of ion pairs *cis*-$Co(en)_2(OH_2)_2^{3+} \cdot H_2C_2O_4/HC_2O_4^-$ to yield $Co(en)_2(ox)^+$ and of *cis*-$Co(en)_2(OH)(OH_2)^{2+} \cdot C_2O_4^{2-}$ to $Co(en)_2$-$(OH)(C_2O_4)$ exhibit a common pressure-independent $\Delta V^{\ddagger}$ of +4.7 cm^3 mol^{-1} which is similar to that observed[32] for exchange of solvent water in *trans*-$Co(en)_2(OH_2)_2^{3+}$ of +5.9 cm^3 mol^{-1}. These observations are most consistent with dissociative release of an aquo ligand as the prime feature of an I_d mechanism, and they contrast with the apparently associative character of oxalate interchange reactions of $Cr(OH_2)_6^{3+}$ which exhibit negative $\Delta V^{\ddagger}$ values.[43]

The reaction of $Fe(CN)_5(3,5-Me_2py)^{3-}$ with cyanide, pyrazine, or imidazole and of $Fe(CN)_5(3-CN-py)^{3-}$ with cyanide yield an average $\Delta V^{\ddagger}$ of +20.6 ($\pm$0.4) cm^3 mol^{-1} (py = pyridine).[44] The large, positive, and nucleophile-independent nature of $\Delta V^{\ddagger}$ is strong evidence for a dissociative (D) mechanism, with effective dissociation of the neutral leaving group from the $Fe(CN)_5^{3-}$ moiety in the transition state. The similarity in $\Delta V^{\ddagger}$ despite substitution by a charged or neutral ligand indicates that the incoming group does not participate significantly in the transition state; otherwise different electrostrictive contributions to $\Delta V^{\ddagger}$ would reasonably be expected for the charged and neutral nucleophiles.

A recent study of the nucleophilic substitution of $Fe(phen)_3^{2+}$ and $Fe(bpy)_3^{2+}$ with hydroxide and cyanide ion indicates a similar primarily dissociative mechanism may be operating.[45] The $\Delta V^{\ddagger}$ values of approximately +20 cm^3 mol^{-1} in each reaction are independent of nucleophile. Either an associative mechanism or a mechanism of direct nucleophilic attack initially on the unsaturated chelate[46] would require appreciable desolvation of the attacking nucleophile from both steric and charge neutralization considerations. The hydroxide ion exhibits a large volume of electrostriction of 22 cm^3 mol^{-1} compared to 8 cm^3 mol^{-1} for the cyanide ion.[39] Since the intrinsic volumes of the ions are similar,[44] both mechanisms should produce positive but distinctly different $\Delta V^{\ddagger}$ for the different nucleophiles. The observation of positive pressure- and nucleophile-independent $\Delta V^{\ddagger}$ values does not favor either of these alternate mechanisms.

Redox Reactions. Two mechanisms for oxidation-reduction involving electron transfer can be considered for metal complexes. The outer-sphere mechanism involving electron transfer without bond-making or -breaking lends itself to a relatively straightforward treatment in predicting $\Delta V^{\ddagger}$ via the quantitative adiabatic theories of Marcus.[47] A detailed analysis of these calculations for a series of electron-transfer systems has been provided in an earlier review.[5] The success of these calculations can be exemplified by the established outer-sphere reaction between $Co(en)_3^{2+}$ and $Co(en)_3^{3+}$ which produced a $\Delta V^{\ddagger}$ (experimental) of -19.8 cm^3 mol^{-1}, compared with a calculated value of -18.4 cm^3 mol^{-1}.[48] For the $Fe^{2+}_{aq}/Fe^{3+}_{aq}$ exchange, the experimental $\Delta V^{\ddagger}$ of -12.2 cm^3 mol^{-1} again is similar to the calculated value of -14.4 cm^3 mol^{-1}, indicating an outer-sphere mechanism. By contrast, the $Fe^{2+}/Fe(OH)^{2+}$ and Cr^{2+}/Cr^{3+} aqueous systems exhibit experimental $\Delta V^{\ddagger}$ which do not agree with predicted $\Delta V^{\ddagger}$ and have subsequently been assigned inner-sphere mechanisms.[5,48]

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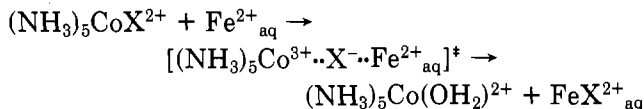(45) G. A. Lawrance, D. R. Stranks, and S. Suvachittanont, *Inorg. Chem.*, 18, 83 (1979).
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An inner-sphere mechanism involves electron-transfer via a bridging ligand, as exemplified by the system

$$(NH_3)_5CoX^{2+} + Fe^{2+}_{aq} \rightarrow$$
$$[(NH_3)_5Co^{3+}\cdots X^-\cdots Fe^{2+}_{aq}]^\ddagger \rightarrow$$
$$(NH_3)_5Co(OH_2)^{2+} + FeX^{2+}_{aq}$$

Should such a reaction proceed by an outer-sphere mechanism a negative $\Delta V^\ddagger$ is predicted. Observed values of +11 (X = F$^-$), +8 (X = Cl$^-$, Br$^-$), and +14 (X = N$_3^-$) cm^3 mol^{-1} have been interpreted in terms of an inner-sphere mechanism with appreciable desolvation of the charged species in the transition state contributing positively to the experimental $\Delta V^\ddagger$.[49] Recently, activation volumes for reduction of Co(NH$_3$)$_5$Cl^{2+} by iron(II) in the presence of sulfate ion show the influence of an iron(II) sulfate pre-equilibrium with a significant variation of $\Delta V^\ddagger$ observed for varying Fe(SO$_4$)$_{aq}$/Fe$^{2+}_{aq}$ ratios.[50] This variation is consistent with inner-sphere reduction by two separate pathways with Fe$^{2+}_{aq}$ or Fe-(SO$_4$)$_{aq}$.

Concluding Remarks

While the topics discussed above encompass recent research endeavors within our laboratories for the application of activation volumes to mechanistic elucidation in reactions of octahedral metal complexes, we can expect the technique to continue to be applied to new areas of mechanistic interest in the future. Although definitive mechanistic evidence will not always be forthcoming from activation volumes, there is now a sufficient body of experimental data accumulating to allow useful mechanistic information to be gleaned from most studies. Certainly activation volume is proving superior to activation entropy as a general mechanistic guide, since $\Delta V^\ddagger$ is usually determined with good precision, and the concept of a volume difference between initial and transition state is amenable to simple mechanistic modelling.

The principal and sometimes severe difficulty in interpretation or prediction of $\Delta V^\ddagger$ lies in an assessment of the size of any electrostrictive component. Since we are usually dealing with ionic species and often with motion of charged ligands in the activation step, electrostrictive components can dominate intrinsic components. It is likely future investigations of the role of the nonleaving groups in series of complexes with common leaving group and metal ion may aid our understanding of electrostrictive effects. Further, studies in a range of both protic and aprotic solvents, where solvation effects should vary considerably, should be of value. Few applications in reactions of organometallic compounds have been reported, and some expansion in this area would be welcome.

The increasing body of experimentally determined activation volumes and reaction volumes, combined with their value in mechanistic elucidation, presage a continued expansion in the study of reactions at elevated pressures in the area of conventional kinetics which is our prime interest. The investigations of activation volumes for octahedral coordination complexes offer more detailed insights into the actual molecular rearrangements occurring during their reactions.

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A Modern Approach to Nonelectrolyte Solubility Theory

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People get interested in solubility theory for one of two reasons. Engineers and applied scientists see it as a means of predicting solubilities in those systems for which data are wanted, but do not exist, and are impractical to obtain. Those among us with more theoretical inclinations would like to know, from the basis of intermolecular forces, why, at any specified temperature and pressure, one substance dissolves in another to exactly the extent that is observed. In this Account we deal with the theoretical aspects of solubility theory;

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in particular, after a preliminary comment we do four main things. First we will go through a bit of history, and in the process point out those early ideas that have found a lasting place in solubility theory. Then we show how recent advances in the theory of liquids has made it possible to quantitatively predict solubilities and related functions from intermolecular forces without using *any* adjustable parameters. Calculations of this kind, even for the very simple systems we describe, were not possible prior to about a decade ago. Following this we show how these calculations can be used both in an approximate way to interpret solubility data in complex systems and in a rigorous way to intercompare theories and to elucidate the influence on solubility made by previously neglected phenomena such as quantum effects and nonadditive intermolecular forces. Finally, we outline some of the remaining problems in the field