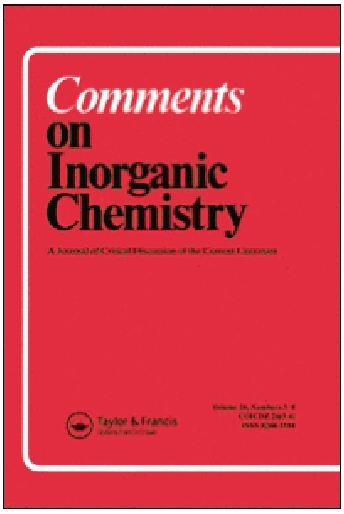

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Analogies Between Coordination and Quaternization of Imines, Including N-Heterocycles

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Analogies Between Coordination and Quaternization of Imines, Including N-Heterocycles

In a Comment on inorganic chemistry, it may seem odd that all the examples contain organic molecules. However, that is because much of the work done in inorganic chemistry laboratories and institutes since the time of Werner has been coordination chemistry, often involving carbonaceous ligands.

Since the initial elaboration of π-cyclopentadienyl chemistry by Fischer and by Wilkinson, organometallic chemistry (even more "organic" in its methods and applications than coordination chemistry) has also become a common field in "inorganic" laboratories. Indeed, it is reassuring that of the 386 pages of volume III of these exegeses, only some 10% were concerned with "classical" (i.e., noncarbonaceous) inorganic systems.

My theme here (by no means new: *vide* the field of "reactions of coordinated ligands") is that at the interface of carbonaceous and noncarbonaceous systems, the effect of the inorganic moiety on the organic is as interesting as the converse. In the area of heterogeneous catalysis, modification of patterns of organic reactivity by coordination to metal ions is often sought and quite often achieved.

The reactivity of unsaturated organic systems is a cornerstone of chemistry. The type of saturation shown in Eq. (1), where X is a moiety (like O or NR) more electronegative than carbon, is used for synthetic purposes chemically and biochemically.

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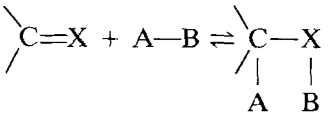


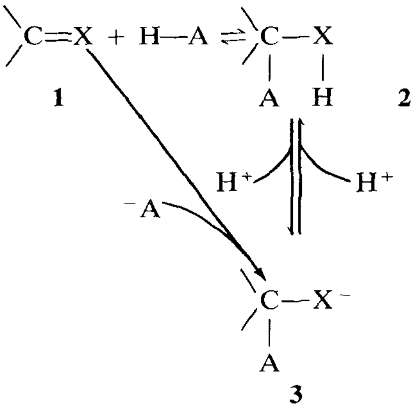
$$\gt C{=}X + A{-}B \rightleftharpoons \gt\underset{A}{C}{-}\underset{B}{X} \qquad (1)$$

For example,[1] though tetrakis-complexes of rhodium(III) with 3-formylpyridine could readily be isolated, in the case of the 4-isomer, covalent aquation of the carbonyl groups occurred:

$$trans\text{-}[Rh(4\text{-}CHO\text{-}py)_4Cl_2]Cl + 4H_2O \rightarrow trans\text{-}[Rh(4\text{-}CH(OH)_2py)_4Cl_2]Cl$$

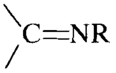
A related finding[2] was that values of K for the addition of water in D_2O at 37 °C to the aldehyde groups of 4-aldehydopyridine, its conjugate acid and its complex with the pentammineruthenium(II) moiety were 0.84, 0.88 and 0.20, respectively, ruthenium(II) being isoelectronic with rhodium(III).

If AB in Eq. (1) is a protic species where say $B = H^+$ and $A = H^-$, Br^- (or other halide or pseudo-halide like CN^- or NCS^-), OR^-, where R may be H or alkyl, OOR^-, NH_2^-, SR^- or the like, then the conjugate base, **3**, of **2** may be known, formed either by acid dissociation of **2** or by direct addition of the nucleophile A to the unsaturated carbon of **1** as shown in Eq. (2).



(2)

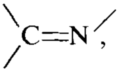
Attention is given here only to the situations where X = NR, that is, imines (R = H), Schiff bases (R = alkyl or aryl), oximes (R = OH) or oximates (R = O$^-$), and the like, and their cyclic analogues, whether aliphatic or aromatic. This aromatic class of compounds containing



$$>C{=}NR$$

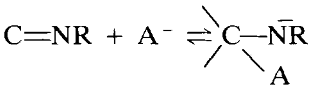
constitutes the huge area of N-heterocycles, including six-membered monoazines (pyridines), diazines (pyrazines, pyrimidines, pyridazines), triazines, five-membered diazines (pyrazoles and imidazoles), thiazoles, oxazoles and the like. Derivatives include such chelating agents as bi-imidazole, bipyrimidyl, and analogues with fused or linked rings like benzimidazoles, 1,10-phenanthrolines, purines and pteridines.

For all molecules containing the imine moiety,

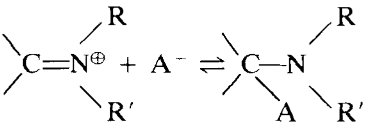


$$>C{=}N<,$$

decreasing the electron density on the nitrogen naturally makes the carbon atom more electrophilic. That is, the equilibrium for the process (4) lies further to the right than that for reaction (3).



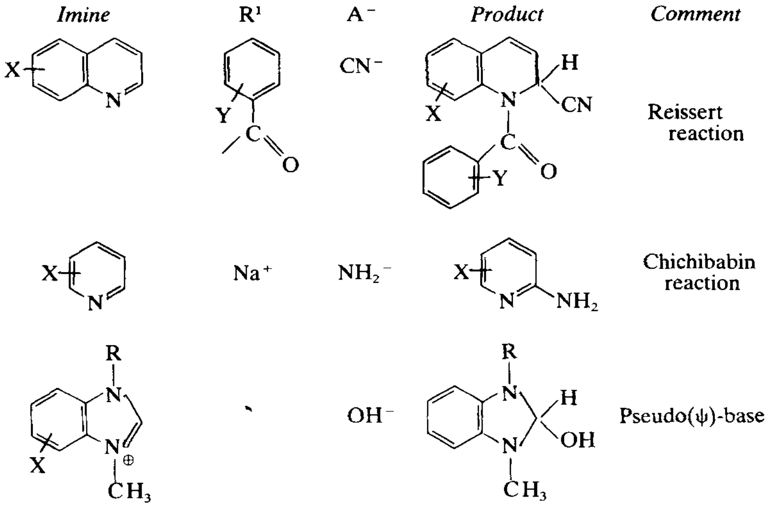
$$C{=}NR + A^- \rightleftharpoons >C(A){-}\bar{N}R \qquad (3)$$



$$>C{=}N^{\oplus}(R)(R') + A^- \rightleftharpoons >C(A){-}N(R)(R') \qquad (4)$$

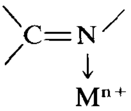
The group R′ which activates the imine bond toward saturation may be of many kinds: some examples are shown in Scheme 1.

The suggestion some years ago that R′ may be a metal ion seems



SCHEME 1

unexceptionable. It does help to account for many properties in the enormous range of compounds containing the moiety **4**.



$$\gt C{=}N\lt \downarrow M^{n+}$$

4

For example, following Westheimer's finding that pyridine catalyzed the oxidation of alcohols by aqueous chromium(VI), these extremely useful chromium(VI) oxidants for alcohols have made a massive contribution to organic synthesis, because it is now often possible to stop at the aldehyde stage. Chromium(VI) (as potassium or tetrakis-n-butylammonium dichromate or other similar systems like CrO_3) is, of course, always a powerful oxidant, whether N-heterocycles are present or not. For example, the famous "volcano" demonstration (Eq. (5)) or the related synthesis of Reinecke's salt $(NH_4)[Cr(NH_3)_2(NCS)_4]$ arise from chromium(VI) oxidizing N(− III).

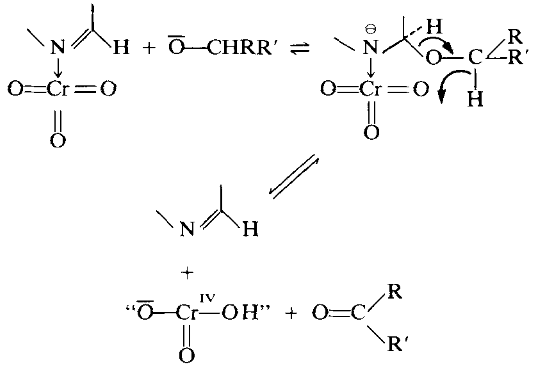
$$(NH_4)_2[O_3CrOCrO_3] \rightarrow N_2 + Cr_2O_3 + 4H_2O \qquad (5)$$

However, the present point is that the N-heterocyclic complexes contain the imine moiety highly activated by chromium(VI) and the probable mechanism for the alcohol oxidation is shown as Scheme 2. The alcohol (probably in the presence of bases, actually alkoxide) has a dual role as a nucleophile and reductant.

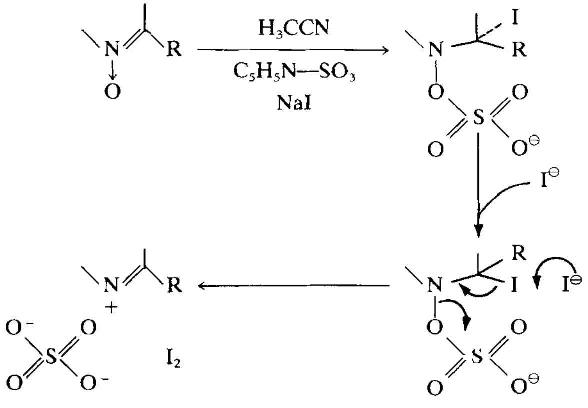
Reagents (each with their peculiar advantages) include Sarett's (py_2CrO_3 in $HCCl_3$), Corey's (CrO_3 and an imidazole in CH_2Cl_2), and several others. The mechanism of Scheme 2 is as consistent with the available facts as those based on the formation of chromate esters, and offers (in addition) an explanation of the fact that the tertiary amine must be an N-heterocycle.

It is worth commenting on pyridinium dichromate, $(C_5H_6N)_2[O_3CrOCrO_3]$, which, following Westheimer's discovery, has been a popular reagent of the type. Several recent papers have discussed its preparation and the like, without acknowledging that it was an article of commerce 50 years ago, sold on a large scale for photographic purposes[3] under the name "Pyrax."

Exactly analogous to the mechanism of Scheme 2 is the suggestion[4] that iodide causes the ready deoxygenation of quinoxaline- and phenazine di-N-oxides as shown in Scheme 3. Other oxidants containing N-heterocycles coordinated to elements in high oxidation states (like the complex $[RuO_2(bipy)Cl_2]$ which cleanly[5] oxidizes



SCHEME 2



SCHEME 3

alcohols to aldehydes) may owe their selectivity to the same cause, intermediacy of a nucleophilic adduct to an N-heterocycle activated by coordination to a metal ion in a high oxidation state, here ruthenium(VI).

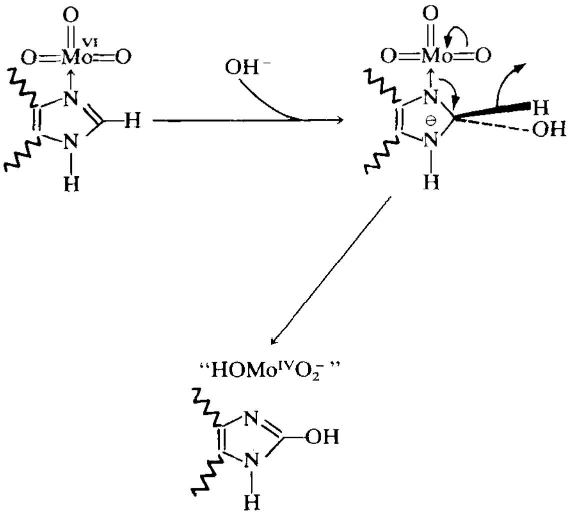
In a similar vein, the two-electron oxidation of xanthine and related substrates by the molybdenum(VI) of xanthine oxidase would fit very much the same pattern, nucleophilic attack of hydroxide upon C(8) of xanthine [activated by coordination of N(7) to Mo(VI)] being followed by hydride transfer, as shown by the partial structures in Scheme 4.

So, a number of comments were made about the possibility of equilibria or preequilibria (like Scheme 5) involving metal ions (other than the known ones in classical N-heterocyclic chemistry, sodium of sodamide in the Chichibabin synthesis and so on).

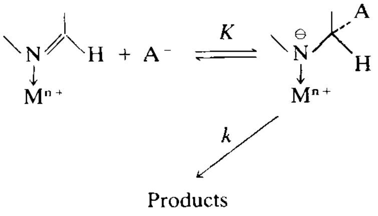
For example[6]: "We suggest that 'quaternisation' by a metal ion may lead to similar low energy pathways for nucleophilic attack by solvent or other Lewis base . . . ."

"Wherever metal ions and N-heterocyclic ligands are together in protic media, the apparent (and invariably assumed) simplicity of the system may in reality, be spoilt by equilibria of the kind we describe here."[7]

Of course, just like some well-known organic examples, *K* or *k* in Scheme 5 may be very small, depending on the particular sit-



SCHEME 4



SCHEME 5

uation. The addition of hydroxide ion to N-alkylpyridinium ions seems to be rather uncommon, whereas the ψ bases of some other N-heterocyclic cations may be crystallized. Cyanide may do better than hydroxide: N-methyl-3, 5-dicyanopyridinium tosylate adds cyanide to give[8] the 1,2-adduct, which above 120 °C rearranges to the 1,4-isomer.

Formation of the new chiral center ("asymmetric carbon") was considered[9] as a possible source of optical activity in rhodium and iridium compounds. Similarly,[10] speaking of the large changes with pH of the electronic spectra of complexes like *cis*-$[Rh(LL)_2(OH_2)_2]^{3+}$, where LL denotes the di-imines phen, bipy and their derivatives, "it was originally suspected that behaviour of this kind in complexes of heterocyclic nitrogen ligands might be due to covalent hydration of the ligand but this has now been shown by NMR measurements not to be a major effect in the present case," and "the NMR spectra . . . with increasing pH, . . . thus providing no evidence for covalent hydration."

Almost at once a comment was made[11] which perhaps explains, in part, why the suggested equilibria (5) have been so vehemently and often unscientifically resisted. It was said that "the chemistry of this important and large group of complexes has been *relegated* [*sic*—my italics] to . . . the organic chemistry of the ligands."

Relegation means the opposite of promotion! There is an obscurantist notion here that "coordination chemistry" is different from and "better" than organic chemistry.

A less circumscribed view of the suggestion that activation of imines by whatever means (organic "quaternization" or inorganic "coordination") is still activation would be that it unites a great swathe of classical N-heterocyclic and imine chemistry with a massive part of their coordination chemistry and biochemistry.

Long-Standing Errors. Unfortunately, there are a number of errors (experiments which cannot be repeated) which have led to dogmatic statements which have not been withdrawn.

(a) Kinetic studies—there are many—have led to the rate law in Eq. (6) for solvolysis (photolytic or thermolytic), cyanide attack, racemization and some other reactions for $[M(LL)_3]^{n+}$, where among studied examples M = Fe, n = 2, LL = bipy or phen, or chelating di-imines (like Schiff bases), and the nucleophile is cyanide or hydroxide.

$$\text{Rate} = [M(LL)_3](k_1 + k_2[\text{Nu}] + k_3[\text{Nu}]^2) \qquad (6)$$

The case of tris-di-imineiron(II) ions reacting with cyanide is of great stereochemical interest. Archer discovered[12] that the optically resolved red ferroin (with one pair of signs of Cotton effect in the "exciton" region: + at long wavelength, − at short) gave the purple *optically active* Schilt–Barbieri compound $[Fe(phen)_2(CN)_2]$ with the opposite signs (− at long wavelength, + at short) as in Eq. (7).

$$\underset{(a)}{(+)[Fe(phen)_3]^{2+}} + 2CN^- \rightarrow \underset{(b)}{(-)[Fe(phen)_2(CN)_2]} + \text{phen} \tag{7}$$

Reaction (7), of course, is one of those where the kinetic pattern of Eq. (6) is followed. The absolute stereochemistry of *a* is known, that of *b* is not, so whether reaction (7) (and the several related extensions[12]) represent one of those rare inversions (observable by polarimetry) of configuration at a kinetically inert tris-chelated metal center is not yet quite certain, though it seems likely. The Schilt–Barbieri compound, *b* of reaction (7), shows a much slower onward reaction to $[Fe(phen)(CN)_4]^{2-}$.

Whatever the mechanism, there is no doubt whatsoever that by reacting resolved ferroin with aqueous cyanide solutions, the optically active dicyano compound forms in good yield. This is indeed the best way to make optically active Schilt–Barbieri species. The fact that reaction (7) is dominant has been demonstrated repeatedly.

Nevertheless, there is a contradictory statement[13] that reaction (7) cannot be observed. The short abstract of that paper begins: "At 25 °C, total loss of optical activity accompanies the rate determining second-order reaction of $[Fe(phen)_3]^{2+}$ . . . with CN^-." This is, quite simply, a wrong observation.

The Schilt–Barbieri compound (apparently a well-understood classical coordination compound) is actually very interesting: its properties reveal the care required before taking up entrenched positions. First, for the optically active species $(+)[Fe(phen)_2(CN)_2]$, addition of Lewis acids causes changes in the visible but not in the UV circular dichroism. For example,[14] reaction (8) occurs:

$$(+)[Fe(phen)_2(CN)_2] + 2Hg(CN)_2 \rightarrow (+)[Fe(phen)_2\{CN\cdot Hg(CN)_2\}_2] \tag{8}$$

The analogous racemic adduct has been crystallized and its structure solved[14] by x-ray diffraction. The stoichiometry is 2 : 1 rather than 1 : 1 as earlier suggested.

Very remarkably, addition of strong protonic acids causes[15] a *shift* of the visible c.d.—like that engendered by such Lewis bases as BF_3—but complete disappearance of the famous UV-c.d. "exciton" bands. These changes are reversible. Second, Schilt's compound isolated as a solid has (at least so far) always been a solvate, for example, $[Fe(phen)_2(CN)_2]\cdot 2H_2O$. Oddly, the water here is not removed thermally[16] until 323 °C, a suspiciously (but not quite conclusively) high temperature for nonconstitutive water. Third, even apparently high quality crystals give only a few reflections (out to $\theta = 10°$) so no structure based on diffraction is yet available.

(b) The idea is commonly advanced that ion pairing is important in giving the preequilibria suggested by the second- and third-order terms in rate equations like (6). There are several equilibrium constants available which cast grave doubt on this, notably for triply charged metal complexes and singly charged anions.

Values have been measured for genuine aqueous ion-pairing equilibrium constants between $[M(LL)_3]^{3+}$ and various anions. Recent Russian work[17] gives values like

$$\begin{gathered}[Ir(phen)_3]^{3+} + X^- \rightleftharpoons [Ir(phen)_3]^{3+},X^- \\ K_{IP} = \frac{[Ir(phen)_3,X]}{[Ir(phen)_3][X^-]}\end{gathered} \qquad (9)$$

$\log K_{IP} = 1.52$ (for $X = NO_3^-$) and 1.22 (for $X = HCO_2^-$).

Ion-pairing "constants" are notoriously dependent on the method employed to secure them, particularly for gegen-ions capable of hydrogen bonding in protic media. Notwithstanding this, values of $\log K_{IP}$ even for $[M(LL)_3]^{3+}$ and OH^- (or CN^-) seem unlikely to exceed 3.0 in water. Indeed, among the few values established from conductance measurement for $[M(LL)_3]^{3+}$ and a singly charged anion, dilute solutions in acetonitrile gave a value[18] of $\approx 10^3$ for $[Co(4,4'\text{-di-}CH_3\text{-bipy})_3]^{3+},ClO_4$, so aqueous values will surely be smaller.

Again, faulty observation has been perpetuated in print. The acid-solvolysis in the presence of chloride ion of ferroin in DMSO has been interpreted as if the species involved were, like those in water, tris-chelate and bis-solvate-bischelate, the kinetic observation being interpreted[19] as arising from ion pairs. Actually, *in that solvent*, the famous aqueous stability of ferroin ($\log\beta_3 = 21.2$) is irrelevant. The blue species $[Fe(phen)_2Cl_2]$ (irrelevant in water) appears[20] in DMSO, with its characteristic spectrum, at the same rate as ferroin disappears!

(c) All agree[21] that both photolysis and thermolysis of Eq. (10)

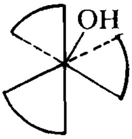
$$[Cr(LL)_3]^{3+} + 2OH^- \rightarrow [Cr(LL)_2(OH)_2]^+ + LL \qquad (10)$$

proceed by formation of a 1 : 1 adduct, and that all subsequent reactions go through this. Unfortunately, the great bulk of detailed kinetic work has been with the tris-2,2′-bipyridyl species: the related studies with tris-1,10-phenanthroline chromium(III) salts are needed. These salts are not altogether easy to make pure: a similar remark applies to several studies of tris-di-imineruthenium(II) species (popular in the solar energy area) made by the reaction (11)

$$cis\text{-}[Ru(LL)_2Cl_2] + LL' \rightarrow [Ru(LL)_2(LL')]Cl_2 \qquad (11)$$

In several published papers, the product—which should of course be orange, with a longest wavelength peak absorption around 460–470 nm—is said to absorb at *ca* 540 nm, a wavelength characteristic of a purple compound, like the dichloro-factor of (11). Such studies, purporting to relate to detailed photomechanisms in the chromophore $[Ru(LL)_3]^{2+}$, should be disregarded.

Returning to the case of tris-bipyridylchromium(III) and similar salts, Serpone, Balzani, and their associates interpreted the kinetics for (10) in favor of short-lived **5** ($t_{1/2} \simeq 10^{-4}$ s!) rather than **6** (both of which are, of course, consistent with the observed kinetics).



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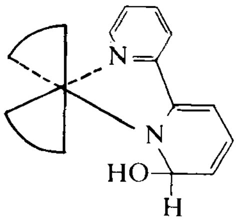
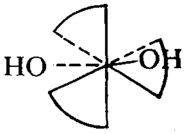


6

An unappreciated but strong argument may be introduced. Many rate laws for nucleophilic (Nu) interaction with imine complexes include terms (often dominant: a typical steep rise occurs at pH > 9, for the $k_2[CrB_3][OH^-]^2$ term) in $[Complex][Nu]^2$. These both demonstrate the existence (so far as this efficient third-order process is concerned) of a 1 : 1 preequilibrium, and further raise the question of the structure of the intermediate for the step involving the 1 : 1 adduct reacting with a second mole of nucleophile (i.e., that giving the third-order term at all). The possibilities are shown as **7**, **8**, **9** and **10**. Species **8**, **9** and **10** would have isomers with the same coordination number at the central metal ion, but with hydroxide attached to other carbon atoms.



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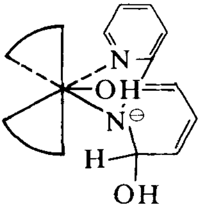

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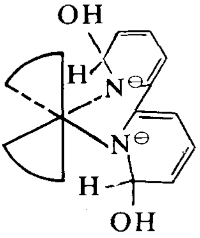

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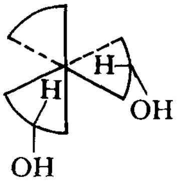


10

The postulation of six-, seven- (structure **5**), and eight- (structure **7**) coordinated chromium(III) species in the same aqueous solution is so inconsistent with classical coordination chemistry as to rule out **7**. No nuclear magnetic resonance studies have been done on these paramagnetic chromium(III) species, and our preliminary ESR experiment in solution was inconclusive. (It did lead to the interesting finding[22] that the ESR spectra of optically active and racemic *solid* $[Cr(bipy)_3]$ perchlorates were utterly distinct. This difference has not previously been noticed for any chiral transition metal compound.) Reverting to the nature of the intermediate species giving the third-order term $k_2[OH^-]^2$, species **9** or **10** seem the more likely.

(d) The base hydrolysis of many six-coordinated cobalt(III) complexes—replacement of chloride, Eq. (12), for example, from $[Co(en)_2B(Cl)]^{2+}$—as in

$$cis[Co(en)_2B(Cl)]^{2+} + OH^- \rightarrow cis\text{-}[Co(en)_2B(OH)]^{2+} + Cl^- \qquad (12)$$

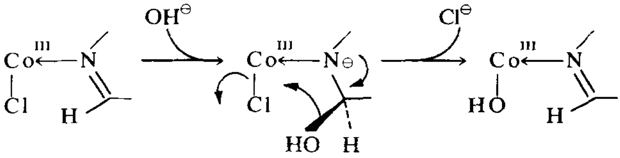
is swift relative to the acid counterpart. The rate law, Eq. (13), for base hydrolysis, one of the few substitutions at metal centers in water to show a second-order term

$$\text{Rate} = k_b[\text{complex}][OH^-] \qquad (13)$$

is usually interpreted as arising from the preequilibrium formation of a conjugate base by deprotonation of an N-H of a ligand. To check this S_N1_{CB} mechanism, a spin-paired d^6 species unable easily to form a conjugate base was studied, with the expectation, of course, that no second-order term would be found. (The question of conjugate base formation is discussed shortly.) Ferroin was chosen, and the well-known rate law for its base hydrolysis discovered (Eq. (6)), with the dominant second-order term!!

That seems odd, even embarrassing, but the difficulty was alleviated, to almost universal satisfaction, by an agreement that the unforeseen result for ferroin must stem from a "special" mechanism. We could, for this particular case, have our cake and eat it! Let us revert to Eq. (13). All rate constants k_b are quite high, but some are unusually so, where B is an N-heterocycle, like pyridine, imidazole, or benzimidazole. One interpretation of that would be the intermediacy of a pseudo base as shown in Scheme 6. It is a pity that rather few base-hydrolysis rate laws and stereochemical patterns are known for $[M(chel)_2BCl]^{2+}$, with M = Cr, Co, Rh, Ir for *both cis* and *trans* isomers. However, a detailed study[23] of *cis*-$[Co(en)_2(C_5D_5N)Cl]^{2+}$ was done to comment on the likelihood of Scheme 6. While it is difficult to gauge the size of any expected secondary isotope effect, there probably should be one if nucleophilic attack occurred at aromatic carbon. None was found: $[k_{proto} = 333 \mp 7\ M^{-1}\ s^{-1};\ k_{deutero} = 335 \mp 8\ M^{-1}\ s^{-1}]$.

However, the results, on cursory inspection, will not bear out that interpretation. Quite apart from the existence of values of k_{proto} (under the same conditions) of 1600 $M^{-1}\ s^{-1}$ from Basolo



SCHEME 6

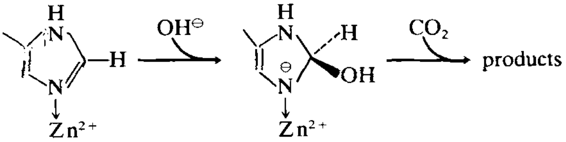
and Pearson, and of 199 from Marty's Swiss laboratory, the quoted rate constants are said[23] to be the *arithmetic mean* (given, for proto, as 333 ∓ 7), of individual values in 6 runs from 310 to 351 M^{-1} s^{-1}, and, for deutero (mean 335 ∓ 8), of 6 runs from 310 to 362 M^{-1} s^{-1}. Confidence limits are supposed to indicate limits of confidence.

The second line of argument was[23] that the pseudo-base mechanism could not apply to imidazoles and benzimidazoles (for which k_b in Eq. (13) is again large, 29 and 220 M^{-1} s^{-1}, respectively) since they have no affinity for nucleophiles! (*sic*). This is quite simply wrong. There is a mass of classical organic work to show that imidazoles, benzimidazoles and their quaternized derivatives form pseudo-bases and the like very readily.

REPRISE

The reactivities toward nucleophiles of the imine function are enhanced when attached to metal ions (which act as if they were "quaternizing agents," turning the nitrogen atom from tertiary to quaternary). This is well known in all manner of contexts. It is worth serious evaluation in any situation where combinations of a metal ion, an imine (di-imine, heterocycle, etc.) and a nucleophile occur. For example, the long-standing argument over the molecular origin of the apparent pK_A (*ca* 7) of carbonic anhydrase has never considered the distinct possibility (stemming from $K_w = [H^+][OH^-]$), that, rather than being a proton loss, this equilibrium could represent a hydroxyl gain, as in Scheme 7.

In this and many other cases, the possibility of the intervention of such species as pseudo-bases, covalent hydrates, 1,2-dihydropyridines and the like may represent a route to increased understanding.



SCHEME 7

NEW FINDINGS

There have been a number of results, in various chemical fields, interpreted by their authors in terms of nucleophilic addition to a coordinated N-heterocycle.

(a) A painstaking study[24] of the solvolyses of the species $[Fe(LL)_3]^{2+}$ by OH^-, where LL = 1,10-phenanthroline (phen) or 4,7-di(disulphonato)diphenyl-1,10-phenanthroline (S-phen), led to the conclusion that "the results are consistent with consecutive reaction mechanism with a reversible step" written as:

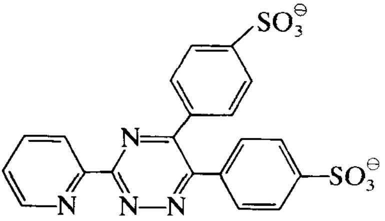
$$[Fe(LL)_3]^{2+} + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Fe(LL)_2(LLOH)]^+ \rightarrow \text{Products}$$

The reversible step, a preequilibrium, had, for its constant,

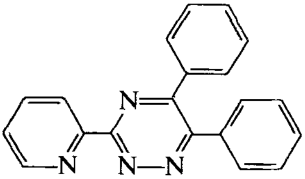
$$\frac{k_1}{k_{-1}} = K = \frac{[Fe(LL)_2(LLOH)]^+}{[Fe(LL)_3][OH^-]}$$

values of 5.0 for S-phen at 25 °C, and 8.4 for ferroin at 5 °C.

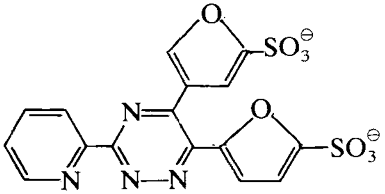
(b) The group led by Blandamer, Burgess and Twigg recently published an extensive survey[25] of their work entitled "Kinetic and Spectroscopic Intimations of Intermediates in Nucleophilic Attack at Di-imine Complexes of Iron(II) and of Molybdenum(0)." This describes many useful properties. The ligands are: bipy, phen, 5-substituted-1,10-phenanthrolines, "ferrozine" **11** abbreviated fz, the corresponding pyridyl-triazine unsubstituted at phenyl **12** abbreviated pp, and a similar disulphonated chelating pyridyltriazine **13** abbreviated fer.



11 (fz)



12 (pp)



13 (fer)

Several ligands (fz, fer) were highly anionic, so that their tris-complexes with iron(II) would be less prone to even that small ion-pair formation found for the cationic complexes.

In favorable cases, it was possible to observe an electronic absorption band due to an intermediate and to follow the disappearance of this and the band from the parent ion as onward reaction occurs, giving equilibrium constants for *reversible nucleophile addition* from absorbance ratios in repeat scan spectra. Better values were obtained by rapid spectrophotometric titration with a strong solution of nucleophile. Table I gives a few representative values.

(c) Moyer and Meyer, in background studies to their interesting novel work[26] on terminal "oxo" species, like the Ru(IV) cation $[ORu(bipy)_2py]^{2+}$ and on its $2e^-$ reduced congener *cis*-

TABLE I

Preequilibrium constants (K in $dm^3\ mol^{-1}$) for $[Fe(LL)_3]^{-4}$ + nucleophile, from Ref. 25

(LL)	Nucleophile	Solvent[a]	Temperature[b]	K[c]
	OH^-	H_2O	298	3.5
$(fz)^{2-}$[d]	OH^-	2 H_2O:1 CH_3OH	298.2	7.0
		1 H_2O:1 CH_3OH	298.2	16
		1 H_2O:1 C_2H_5OH	298.2	230
$(fer)^{2-}$[e]	OH^-	H_2O	298.2	50
	CN^-	H_2O	298.2	5

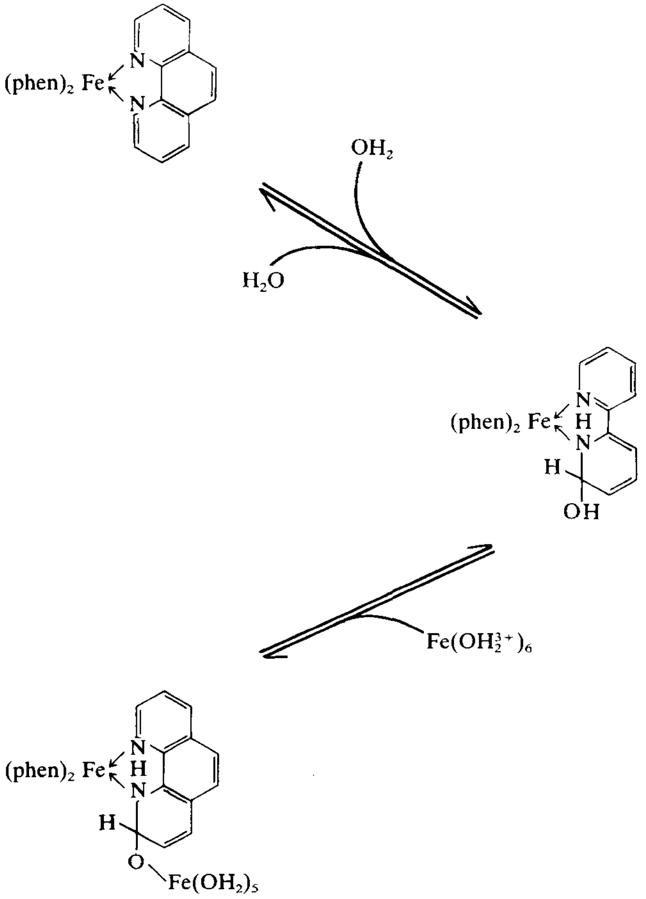
[a] By volume.
[b] °K.
[c] $[Adduct][Complex]^{-1}[OH]^{-1}$.
[d] Formula (**11**) of text.
[e] Formula (**13**) of text.

$[(bipy)_2Ru(py)(OH_2)]^{2+}$ made several observations relevant to the present theme. For example, oxidation of *cis*-$[(bipy)_2(py)Ru(OH)]^+$ with alkaline (0.1 M NaOH) permanganate "showed that a large number of oxidizing equivalents (approx. 14, assuming 3 equiv mol^{-1} of MnO_4^-) are required to remove completely the . . . peak at 505 nm. These results point to a complicated and extensive chemistry involving oxidation of the organic ligand." The percipient remark was made that "just as in quinone chemistry, nucleophilic attack by OH^- ion may render the phen or bipy ligand . . . further oxidations." Permanganate, of course, contrary to long-standing fable, oxidizes pyridine rings perfectly well in alkali[27] or acid[27,28]: Chichibabin himself[29] converted benzylpyridine, 2- and 4-phenylpyridines to benzoic acids in *alkaline* permanganate.

(d) Schmid and Han, working in Vienna, realized[30] that a number of reactions of di-imine complexes showed the remarkable phenomenon of anti-compensation, impossible for a single-step reaction. They therefore analyzed their kinetic results on the reduction (14)

$$[Fe(phen)_3]^{3+} + [Fe(OH_2)_6]^{2+} \rightarrow [Fe(phen)_3]^{2+} + [Fe(OH_2)_6]^{3+} \tag{14}$$

in terms of the two steps shown in Scheme 8.



SCHEME 8

(e) Table II, taken from a recent collection[31] by Clack and me, shows how the rate of base hydrolysis represented by k_2, the constant in the second-order term of base hydrolysis, correlates not too well with electron densities in iron(II) orbitals, and is in as good relation with charges on carbon atoms adjacent to imine nitrogen. Indeed, where (as in the complexes of bipyridinazyl) there is *no* such carbon atom, the rate becomes remarkably slow.

TABLE II

Calculated orbital occupancy (INDO) for Fe and charges ($\times 10^3$) for carbon, with rate constants (k_2 of Eq. (6) in text) for $Fe(LL)_3^{2+}$ base hydrolysis

	d_σ		d_π		d_σ			
Ligand	$3d_{xy}$	$3d_{xz}$	$3d_{yz}$	$3d_{x^2-y^2}$	$3d_{z^2}$	k_2	C_6	Σ^a
phenanthroline	0.35	1.86	1.56	1.93	0.57	6×10^{-3}	137	6.269
4,4′-bipyrimidine	0.36	1.90	1.43	1.94	0.59	–	287	
2,2′-bipyrimidine	0.33	1.87	1.61	1.93	0.56	386	187	6.291
3,3′-bipyridazine	0.37	1.87	1.48	1.94	0.59	3.3×10^{-5}	−69(N)	6.248
2,2′-bipyrazine	0.36	1.87	1.53	1.94	0.57	328	94	6.270
2,2′-bipyridine	0.36	1.89	1.46	1.93	0.59	2.9×10^{-3}	133	6.226

[a] d-occupancy, the sum of d_σ and d_π.

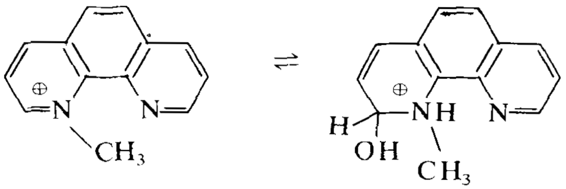
The calculations (to save computer time) are for $[Fe(LL)(CN)_4]^{2-}$, using the INDO method, and we assumed that the results could be transferred to $[Fe(LL)_3]^{2+}$. In Table II, because of the framework axes chosen, the division into "t_{2g}" and "e_g" sets is not the familiar one with $d_{x^2-y^2}$ and d_{z^2} as the e_g pair, but the results are equivalent.

(f) The facts of a number of similar suggestive observations are fairly well summarized in a recent review,[21] except that the significance of observations on optical activity is generally omitted: one such case is therefore described here, that of the Pfeiffer effect.

THE PFEIFFER EFFECT

The Pfeiffer Effect is a case of dissymmetric induction. When a racemic tris-chelated species $[\alpha]_\lambda = 0$ is left to come to equilibrium in an aqueous medium containing an optically active kinetically stable ion, $[\alpha]_\lambda = x$ (often called the environment compound), the final rotation is not the sum of the original ones $[\alpha]_\lambda = x + 0$, but has a new value, y. Pfeiffer's original observations were made with tris-di-imine complexes like $Zn(phen)_3^{2+}$. To this day, *cationic* Pfeiffer compounds and *cationic* environment compounds (usually alkaloid cations, like strychninium) are found to show Pfeiffer effects *only* when the racemic compound contains chelating di-imine ligands, e.g., $Zn(bipy)_3^{2+}$, $Ni(phen)_3^{2+}$. To restate this, the fascinating cation : cation Pfeiffer effects are a property of N-heterocyclic complexes only.

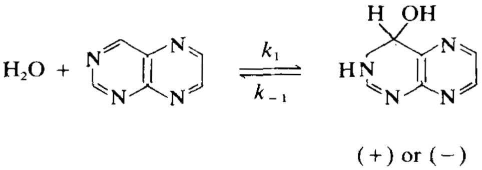
Some fairly new facts[32] have not yet been generally absorbed into the corpus of information on the cation : cation Pfeiffer effect. When the iodide of N-methyl-1,10-phenanthrolinium (**14**), surely a flat cation, is added to an aqueous solution of a chiral alkaloid salt, the biggest known "Pfeiffer rotation" (y-x above) develops at equilibrium.



14 **15**

Chirality must develop in **14** from the development of one or more new elements of asymmetry such as in **15**. There is a very suggestive analogy (albeit with a *kinetic* property) with the stereoselectivity of adenosine aminohydrolase, which catalyzes the covalent hydration/dehydration of [inter alia] flat pteridine, as shown in Scheme 9. $K_+ = K_- = 6.9$, but $k_{1(-)} > k_{1(+)}$, so the ($-$) hydrate forms (initially) more rapidly.

The present suggestion is that it is the differing diastereoisomeric combinations possible among the covalently hydrated and pseudobasic complexes with their dissymmetric environment which generate the Pfeiffer effect.



SCHEME 9

Structural work to distinguish the isomeric species with seven-coordinated metal ions from those with six-coordinated metal ions and one or more carbons of the ligand with covalence expanded from three to four has been an obvious next step for some 20 years. This structural work will almost certainly involve diffraction studies of single crystals.

The need will remain to recall that, in systems at labile equilibrium, with rates of interconversion of solution species comparable to those of nucleation and crystallization, the crystallizing solid may not necessarily contain the dominant solution species, or even a major one. One of the more common errors in aqueous chemistry is now this assumption, *unproven*, that one may use solid structure of a species from a crystallizing solution to comment on speciation in that solution. For bisaminoacidato-copper(II), the aqueous solutions (with their very rapid equilibrations) have been assumed for many years to contain *trans*-isomers only. Indeed, for L-alaninate, the *trans*-bis-isomer crystallizes: leave it under the mother liquor for several days, and the solid *cis*-isomer replaces it. For glycinate, very similar phenomena occur, except that now it is the *cis*-isomer which crystallizes first.

A major problem (causing great fascination in other contexts, but at present unhelpful here) is that different solvates (with very different properties) are extremely common among salts of complexes of imines (including N-heterocycles) with metal ions, and polymorphism is common among the solvates. For example, Drago found that racemic $[Ru(bipy)_3](PF_6)_3$ crystallized as a stable $0H_2O$, and "unstable" $2H_2O$ and $6H_2O$. We similarly—with optically active $[RuP_3]^{3+}$—crystallized a green anhydrous perchlorate and a *purple* monohydrate (spectroscopically quite distinct, though both could be reconverted quantitatively to salts of the orange tris-1,10-phenanthrolineruthenium(II) ion). Similarly, solvated tris-1,10-phenanthrolinenickel(II) salts, whether resolved or racemic, show a range of polymorphism which often leads to discrepancy in reported properties. In passing, it is vital in describing properties of solid substances that the particular solid phase(s) used should be identified so that others may follow.

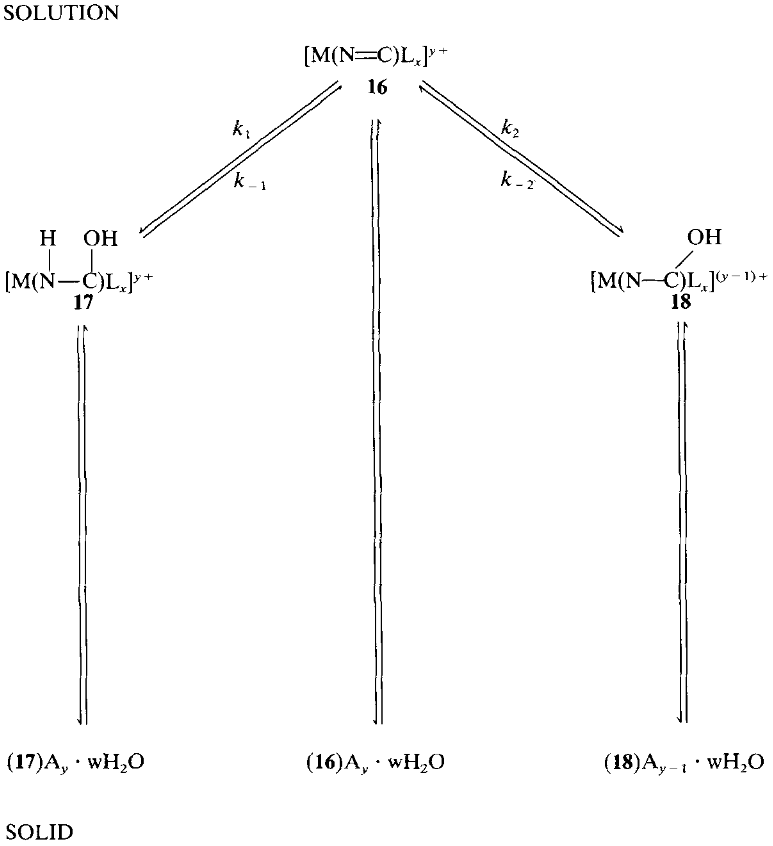
Typically, following an early value[33] of 8 for the equilibrium constant for water adding to the $[Ni(phen)_3]^{2+}$ ion in 1,2-dichloroethane, the remarkable sensitivity of the c.d. of the ion to water activity was demonstrated.[34] There are[35] at least five polymorphs of DL-$[Ni(phen)_3]I_2 \cdot xH_2O$ (x = 2 or 3) which interconvert fairly readily, some having only short half-lives. We studied (*faute de mieux*) the crystal structure[35] of the *most* stable form, to which the others converted or reverted. This (perhaps unsurprisingly) contained hydrogen-bonded sheets of water.

The salt *trans*-$[Ir(py)_4Cl_2]Cl \cdot 6H_2O$ may crystallize in two forms from water. One (the "higher temperature form"), assembles in good-looking crystals of unhelpful morphology around 25 °C. The other form, which crystallizes around 2 °C, has[35,36] an interesting structure involving the usual four-bladed propeller on the halide-metal-halide spindle for the cation, and a neatly hydrogen-bonded sheet of water molecules interspersed between the cations.

In neither structure is there covalent modification of any carbon atom. In early attempts to discover the nature (7-coordinated or covalently hydrated?) of the adducts with solvent of chromium(III) complexed by imine structures, neither [Cr(2,2′,2″-terpy)$_2$]$(ClO_4)_2 \cdot 2H_2O$ nor $[Cr(bipy)_2Cl(OH_2)]Cl_2 \cdot xH_2O$ contained[21] any 4-coordinated covalently hydrated carbon atoms, nor any 7-coordinated metal ions either. The weight to be attached to such *negative* findings is tiny. There were, at one time, no compounds of xenon, no perbromates, no carboranes, and so forth, and general statements were often made, based on their "nonexistence."

The problem in *heterogeneous* equilibria is shown in Scheme 10. Depending upon pH, the rate and/or equilibrium constants, and the solubility products, any of (**16**)A_y, (**17**)A_y and (**18**)A_{y-1}, or of their hydrates may crystallize. So, the fact that in the fairly numerous known structures $[M(N{=}C)L_5]A_n \cdot wH_2O$, no covalent hydrate or pseudo base has yet turned up signifies about the same as that no 7-coordinated metal ion has turned up either.

There are several "obvious" pseudo-base structures to do. When aqueous hydroxide is added to the red aqueous solution containing the tris-complex of **12**, $[Fe(pp)_3]^{2+}$, a new absorption band appears, then a *blue* precipitate,[25] probably containing $[Fe(pp)_2(ppOH)]^+$ ions. It reverts to red readily (H_2O, CH_3OH, C_2H_5OH), but gives blue solutions in higher alcohols (propan-1-



SCHEME 10

ol, butan-1-ol) where the color disappears only slowly (first order). As in other cases, the problem is to get good-quality crystals.

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