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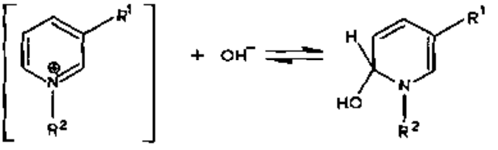
LETTER TO THE EDITOR

Dear Sir,

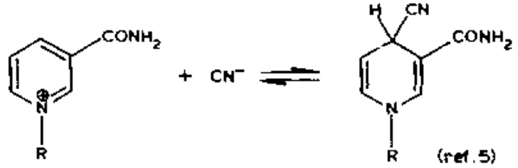
Thank you for your letter of November 29th, 1982, inviting me to discuss the content of Dr. Serpone's article [1] within the framework of my own approaches to the problem.

First, I will restate my analogy between the modification of reactivity which occurs in *N*-heterocycles on complexing with metal ions, as compared with quaternization by classical organic moieties. Secondly, I will describe this analogy in terms of coordination numbers. Thirdly, I will exemplify some systems where there is evidence that the possible presence of pseudo-base-type equilibria or intermediates should be considered. These examples come from laboratories in Wales and elsewhere; several seem not to have been noticed in the review by Dr. Serpone and his several co-authors. Finally, I shall repeat a summary recently given in another critical review [2] of my work.

Classical heterocyclic chemistry accepts that quaternization of *N*-heterocycles leads to an increase in susceptibility towards nucleophilic attack in at least some positions in the ring. This subject has been magisterially surveyed [3] recently. Despite the rather surprising lack of quantitative work, examples of equilibria involving addition of certain nucleophiles to carbon atoms in the quaternized ring are well documented. For example:



R^1 = CN, R^2 = alkyl, benzyl: (ref.4)



Examples are known for monazines, diazines, triazines, and for five-membered heterocycles. For example:

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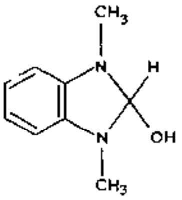


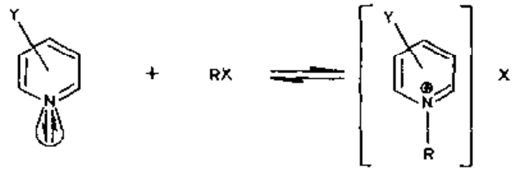
In the case of benzimidazole, discussed [6] in the context of the swift base hydrolysis of $[Co(en)_2(benzimidazole)Cl]^{2+}$, the very existence (well known [7] in organic laboratories working on quaternized benzimidazoles) of these pseudobases of *quaternized* imidazoles was flatly denied, the 'authority' being an elementary text [8].

These *N*-heterocycles have been dominant as ligands and components of chelating ligands in coordination chemistry. Metal complexes of such *N*-heterocycles are important in many fields including (among many others): (i) analysis; (ii) photochemical activation of water, where ruthenium(II) complexed by 2,2′-bipyridyl and similar ligands is currently paramount; (iii) antibacterial effects — Dwyer showed the utility of such complex species as tris-5-nitrophenanthrolineruthenium(II), and the anti-bacterial activity, extensively studied here, of rhodium complexes with *N*-heterocyclic ligands is remarkable; (iv) mechanistic studies, where such complex ions as tris-bipyridylosmium(II) are viewed as well-defined redox agents; (v) metallo-enzyme centres, where imidazole is commonly a ligand of active metal centres (for example in carbonic anhydrase, the active zinc ion is bonded to three imidazole residues of histidine in the apo-protein); (vi) spin crossover studies in a number of solid compounds such as di-isothiocyanatobis-1,10-phenanthrolineiron(II); (vii) pressure effects on magnetic behaviour, as in the extraordinary results obtained by Drickamer on hydrated tris-phenanthrolineiron(II) salts; and (viii) possible catalytic activation of *N*-heterocycles, as in $C_5H_5N + D_2O \rightleftharpoons C_5H_4DN + HOD$, catalysed (heterogeneously) by Group VIII metals.

The novel suggestion which is at the heart of my research in this field is the following.

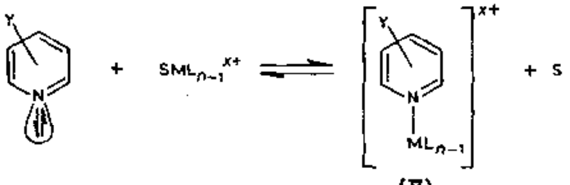
The effect on the reactivity of N-heterocycles caused by binding to metal ions (coordination) will be similar in kind to the effects of bonding the N-heterocycles to other charge acceptors, such as alkyl or aryl groups (quaternization).

That is



(I)

(where positions 2, 4 and 6 of the heterocycle are *known* to be activated to nucleophilic addition) is compared with



(II)

and the analogy made that positions 2, 4 and 6* in (II) will be activated similarly to those in (I).

One critical distinction between 1 : 1 covalent addition (whether its reality is deduced on kinetic, thermodynamic, or spectroscopic grounds) of a nucleophile to aromatic species like (I) as against metal complexes like (II), is that in (I), the coordination number of carbon undoubtedly changes from 3 to 4. In (II) however, *either* that may happen *or* the coordination number of the metal may increase to 7 (for an octahedral II) or to 5 (for a planar or tetrahedral II).

This analogy (that in II, it is indeed aromatic carbon whose coordination number increases) of course unites whole swathes of inorganic coordination chemistry and organic heterocyclic chemistry. Several laboratories have found evidence in its support since I first gave a detailed statement [9] in this journal in 1975 (following my original comment [10] in 1969). A few examples are listed.

(i) Burgess and his school have observed some intermediate species arising from nucleophilic attack of cyanide or hydroxide on coordinated di-imines $[Mo(CO)_4(5NO_2phen)] + CN^-$ [11a]; ferrozine [11b]; $[Mo(CO)_4(bipy)] + CN^-$ [11c].

(ii) "Observations (on the luminescence quantum yield of $[Ru(bipy)_3]^{2+}$ in clay membranes) were taken as evidence [12] that covalently hydrated or slightly distorted bipy ligands are formed". Other explanations are in my own view also as likely here.

(iii) In electrochemical work, Brisset [13] has suggested that equilibria observed at high pH for solutions of $[Fe(CN)_5(Nhet)]^{3-}$ stem from addition of hydroxide to the *N*-heterocycle as in

$$[Fe(CN)_5L]^{3-} + OH^- \rightleftharpoons [Fe(CN)_5(L.OH)]^{4-}$$

(L = pyrazole) [13a] (L = pyridines) [13b]

(iv) Vanderhooft and Ernst [14] found that the reaction of 2,2′-bipyridyl

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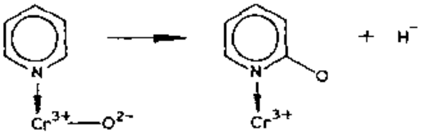
* The actual position(s) of attack will vary from case to case.

with tetrakisallyl uranium(IV) gave complexed mono- and di-allyl-2,2′-bipyridyl (various isomers). Ernst believes that this happens by way of nucleophilic attack of allyl carbanions on bipyridyl coordinated to uranium.

(v) Japanese workers very recently discovered [15], using detailed infra-red spectra (with isotopic labelling), that there is nucleophilic attack, as shown by surface oxides in Cr_2O_3, on the 2-position of pyridines coordinated to chromium(III).

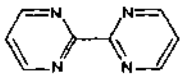
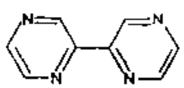
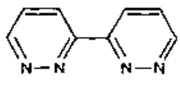


In my own research group, a number of systems have been studied. A few results are listed.

(i) Accepted mechanisms for acid hydrolysis of $[M(LL)_3]^{n+}$ (LL = chelating di-imine) require an *increase* in rate with increasing acidity of the medium.

The rates of dissociation of $[Ni(bipy)_3]^{2+}$, $[Fe(bipy)_3]^{3+}$, $[Fe(phen)_3]^{3+}$, $[Fe(terpy)_2]^{3+}$, $[Fe(5\text{-}Cl\text{-}phen)_3]^{3+}$ and $[Fe(5\text{-}Br\text{-}phen)_3]^{3+}$, and the rates of racemization of $(+)[Fe(bipy)_3]^{3+}$ and $(+)[Fe(phen)_3]^{3+}$ in concentrated sulphuric acid are close to *zero*.

(ii) Among the isoelectronic tris-diazine complexes $[Fe(LL)_3]^{2+}$, the rate constants for hydrolysis are, with structures:

LL	k_{H_2O} (s^{-1})	k_{OH^-} ($dm^3\ mol^{-1}\ s^{-1}$)
	?	386
	4×10^{-3}	328
	~ 0	3.3×10^{-5}

Roughly speaking, I see the much reduced rate of solvolysis of the tris(bipyridazine)iron(II) as arising from the lack of an electrophilic carbon atom at the 2-position of the heterocyclic ring.

(iii) Salts of $[Pt(py)_4Cl_2]^{2+}$ are acidic in water. This we attributed to the equilibrium

$$[Pt(py)_4Cl_2]^{2+} + OH^- \rightleftharpoons [Pt(py)_3(py.OH)Cl_2]^+$$

The fact of acidity (previously noticed by Grinberg [16]) has been denied [17], but, to quote from Constable's review [2], its reference 181 (a personal communication from Seddon and Turp) "recent results suggest the highly purified complex gives acidic solutions, and that the pH falls before chloride ion is released". The analogous compound of 4-methyl-pyridine behaves similarly.

Indeed, in a very old-fashioned experiment, I find that *freshly prepared* solutions of the pure salts cause methyl orange but not litmus to change colour. The extensions of this to accurate evaluation of apparent pK_a, even for rather labile complexes, are clear.

(iv) The electronic, c.d. (where relevant), and NMR spectra of many molecules show rapid and reversible changes with pH. $[Ru(5NO_2\text{-phen})_3]^{2+}$, *cis*-$[Ru(LL)_2(R\text{-py})_2]^{2+}$ (LL = bipyridyls and phenanthrolines) and $[Ru(TPT)_2]^{2+}$ (TPT = 2,4,6-tri(2-pyridyl)-1,3,5-triazine) are examples.

There is then some evidence for this new theory (that coordination is a form of quaternization). However, partly because of the ambiguity in interpreting second-order kinetic terms in solvolysis, partly because detailed studies of the addition of cyanide to the four-coordinate ion $[Pt(1,10\text{-phen})_2]^{2+}$ clearly show that a *five*-coordinated adduct with cyanide may be crystallised as its perchlorate and partly for other reasons, the suggestion has been hotly denied.

Indeed, one paper [18] went so far as to say that "the chemistry of this important and large group of complexes has been relegated (sic) to... the organic chemistry of the ligands", by observations of the kind described here. A more neutral view is taken by Constable in his review [2]. He says, in essence, of the *octahedral complexes*, that:

(a) there is good evidence for nucleophilic addition to ligands based on diazines and triazines;

(b) there is good evidence for such addition in 5-nitro-phenanthroline (with its electron-withdrawing substituent); and

(c) there is no unequivocal evidence in the cases of bipyridyl and phenanthroline.

In addition, he says that the evidence, in the planar cases (four-coordinate), favours the addition to the metal, to give five-coordinate metal ions.

To use Constable's words once again, "It is... more likely that the stronger nucleophiles do attack bipy and phen ligands coordinated to transition metals, and this provides an opening into a new, and very interesting area of chemistry. To quote Gillard '... the link between one major branch of inorganic chemistry and a major branch of organic chemistry seems likely to offer useful explanations for... phenomena in the highly important systems involving an *N*-heterocycle, a metal ion, and a nucleophile...' ".

Positions seem to have become entrenched, and that is always a mistake in a rapidly changing area of chemistry. Let me say that Constable's conclusion [2] seems more reasoned than that in your journal [1], and my own view is what it always was, that such a grand generalization, uniting two great areas of chemistry, deserves proper evaluation.

In some cases, e.g. $[Pd(Hoxine)_2(CN)_2]$ we have found no evidence for covalent addition of nucleophile (here CN^-) to ligand, and in other cases, e.g. $[Ptpy_4Cl_2]^{2+}$ we and others have found good evidence for it (with OH^-).

I enjoyed reading the review [1] of my theory and extensive experiments.

May I conclude by reminding you of a really classical quotation [19], the translation is from a paper by Riddell and Robinson [20]: "weed of... natural philosophy brought forth again by pseudo-scientists who try to smuggle it like a fashionably dressed and freshly rouged prostitute into good society where it does not belong".

That remark may have given offence in its time I suppose, but now, 100 years later, seems merely incoherent.

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