Complexation of Pd(II) with Nucleosides. Evidence for a Strong Interaction Pd···HN by NMR

DIMITRI CAMBOLI, JACK BESANÇON, JEAN TIROUFLET, BERNARD GAUTHERON and PHILIPPE MEUNIER

Laboratoire de Synthèse et d'Electrosynthèse Organométalliques associé au CNRS (L.A. 33), Faculté des Sciences, 6 bd. Gabriel, 21100 Dijon, France

Received December 30, 1982

The initial discovery of Rosenberg [1] has led to extensive studies concerning the interaction of metals and in particular of Pt(II) with nucleic acid constituents. The structure of some complexes has been established by crystallographic data and the main results show many variations about the site of coordination [2]. The pentose moiety has no determinative role in the coordination. But the bases have many sites of binding: heterocyclic nitrogen, amidic nitrogen and oxygen atoms [2]. For nucleotides, the divalent ions can also show interactions with phosphate groups [3]. In our opinion, a systematic approach must be conducted in a stepwise manner and necessitates progressive comparative studies of the behaviour of free bases, nucleosides and nucleotides and if necessary, the same molecules bearing protective groups.

This note provides some preliminary results concerning the products obtained in the reaction of K_2PdCl_4 and $K_2Pd(SCN)_4$ with: a) free bases; adenine (Adi) I, methylcytosine (MeCyt) II. b) nucleosides; 2-deoxy-adenosine (deo-Ado) III, 2-deoxycytidine (deo-Cyd) IV and guanosine (Guo) V. c) a protected nucleoside; N-benzoyl 2-deoxycytidine (N-benz-deo-Cyd) VI.

The palladium complexes are obtained by mixing in aqueous medium the free base, the nucleoside or the protected nucleoside with K_2PdCl_4 or $K_2Pd(SCN)_4$ in the respective stoichiometry 2/1. After heating the solution at 50 °C, a microcrystalline yellow complex is usually formed. It is washed carefully and dried. The analytical results show that, in all the isolated complexes, the metal is always coordinated with two organic ligands. It appears that the nature of these complexes varies with the ligand.

The complexes I′, II′, III′, IV′ and V′ (Table I) (which are related respectively to the organic ligands I, II, III, IV and V) are insoluble in most solvents and are of a covalent nature. They correspond to the general formula (PdL_2X_2) (where L is monodentate). When the ligand X is CNS, the $\nu_{C\equiv N}$ absorption ($\cong$2000 cm^{-1}) is typical of complexes having a metal–sulfur bond. Therefore it appears that important modifications on the basic ligand do not affect the stoichiometry of the complex.

Moreover a *trans* configuration seems the most likely for all the complexes because the IR spectrum of I′ and IV′ shows only one Pd–Cl stretching band near 350 cm^{-1} [2d] and the SCN ligands usually adopt a *trans* geometry [4].

The complex V′ which is formed by guanosine V is soluble in water. It corresponds to an anionic species $(PdL_2)X_2$ (where L is bidentate) and the chloride ion is easily detected in the water solution of this complex.

The comparison of NMR and IR data between the two kinds of complexes and the corresponding free ligands affords specific information about the site of complexation and the complete structure of the complexes.

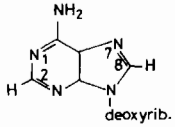
In the discussion of these results, we can assume that the electronic perturbing effect of the palladium atom will be in strong correlation with the identity or the proximity of the atoms or groups involved in the complexation. First of all, it can be seen (Table I) that the palladium complexes of methylcytosine II′, deoxycytidine IV′ and N-benzoyldeoxycytidine VI′ are coordinated only through the N(3) nitrogen atom since the complexation has very little effect on the $\nu_{C=N}$ vibration. Another important feature of complexes II′ and IV′ is an outstanding modification of the NMR signal of the two NH_2 protons. These two protons in the complexes are highly deshielded ($\Delta\delta > 1{,}4$ ppm) compared to the free ligand and they are non-equivalent.

This non-equivalence cannot be attributed to a diastereotopy due to the presence of the asymmetric pentose group in IV′ because it is effective for the methyl cytosine complex for which this chiral group is absent. Moreover, the non-equivalence does not occur for the uncomplexed basic ligands IV and III and it would be difficult to postulate so large an enhancement of the diastereotopy by the simple effect of the complexation to the palladium atom. In our opinion, the observed non-equivalence can only be attributed to a selective interaction between the palladium atom and one hydrogen of the amino group. The possibility of such an interaction has already been postulated between palladium as well as molybdenum and CH_3 groups [4]. It seems difficult to account for the fundamental nature of this interaction but it is clear that one of the hydrogen atoms remains in the vicinity of the anisotropic area of the palladium atom.

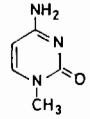
By studying the variation of NMR spectra of the NH_2 signal with temperature we can estimate the corresponding energy of activation to be 80 KJ

0020-1693/83/$03.00

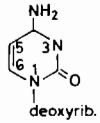
TABLE I. Main Characteristics of the Complexes.



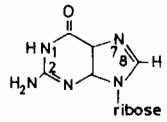
2-deoxyadenosine (deoAdo) III
adenine (Adi) I



methylcytosine
(MeCyt) II



2-deoxycytidine (deoCyd) IV
N-benzoyl(deoCyd) VI



guanosine (Guo) V

Compounds[b]	NMR δ ppm, 25 °C, $(CD_3)_2SO$[e]						IR (cm^{-1}, ICs)[c]		
	NH	H_8	H_6	H_5	H_2	NH_2	$\nu_{C=O}$	$\nu_{C=C}$ $\nu_{C=N}$	ν_{Pd-X}
Adi (I)		8.11			8.09	7.11		1605, 1500, 1420	
$(Pd(Adi)_2Cl_2)$ (I′)								1600, 1465, 1415	340 (Pd–Cl)
MeCyt (II)	3.18(CH_3)		7.54(d)	5.59(d)		6.94	1665[a]	1630	
$(Pd(MeCyt)_2SCN_2)$ (II′)	3.30(CH_3)		7.76(d)	5.90(d)		8.40	1660[a]	1620[f]	2065, 2106
						8.74			(SCN)
deoAdo (III)		8.33			8.13	7.34		1690, 1612, 1570	
$(Pd(deoAdo)_2SCN_2)$(III′)		9.08			8.49	8.90[a]		1670, 1605, 1565	2065, 2125 (SCN)
deoCyd (IV)			7.79(d)	5.72(d)		7.14	1664	1620, 1538, 1500	
$(Pd(deoCyd)_2Cl_2)$ (IV′)			7.98(d)	5.93(d)		9.38	1660	1610[f], 1535, 1490	352 (Pd–Cl)
						8.40			
Guo (V)	10.66	7.90				6.48	1730	1630, 1570	
$(Pd(Guo)_2Cl_2)$ (V′)	10.80	7.96				6.62	1695	1605, 1540	
N-benz.deoCyd (VI)	11.24		8.40(d)	7.34(d)	7.60–8.00 (C_6H_5)		1696[g]	1626, 1562, 1505	
							1640		
$(Pd(N\text{-benz.deoCyd})SCN_2)$	11.79		8.78(d)	7.36(d)	8.40–7.80 (C_6H_5)		1700[g]	1617, 1563, 1495	2062, 2128
(VI′)							1652		(SCN)

[a]Broad band or signal. [b]Analytical results are in good agreement with the molecular composition proposed. [c]Perkin Elmer 580 B spectrograph. [d]Doublet. [e]JEOL FX 100 spectrograph. [f]Weak. [g]Benzoyl group.

mol^{-1}. This value is of the same order of magnitude as the energies which have been found for Pd···HC and Mo···HC interactions [5].

It seems unlikely that the high value found in our case results from the partial double bond character of the C–NH_2 bond possibly enhanced by the complexation (such an activation energy is reported to be about 25 KJ mol^{-1} [2a, 8].

For deoxyadenosine complex III′, the high deshielding of H(8) and the bathochromic effect on $\nu_{C=C}$ and $\nu_{C=N}$ show that the coordination of the palladium atom is through the N(7) nitrogen atom. But in this case the NMR signal of the two NH_2 protons is not split at room temperature. It can only be noted that a significant shift and an appreciable broadening is observed compared with the signal of the free nucleoside. This broadening indicates that the coalescence occurs at room temperature and corresponds to a weak interaction between palladium and the NH_2 group. This fact is a direct consequence of the distance of the NH_2 group with regard to the coordination site. The only suitable solvent for this complex is DMSO which does not allow for low temperature studies. The complex I′ (from adenine) is insoluble in the usual organic solvents and we cannot obtain any significant results from the NMR data. The corresponding IR data ($\nu_{C=N}$ frequency) are consistent with a coordination on the N(7) nitrogen atom.

Lastly, all the spectroscopic data obtained from the complex V′ of guanosine are in good agreement with the ionic character of a bidentate complex $(PdL_2)X_2$. The Pd–Cl vibration is not observed and there is a substantial bathochromic effect on $\nu_{C=O}$ and $\nu_{C=N}$. Moreover H(1) and H(8) protons are deshielded. These results indicate a chelating interaction between the metal, the oxygen atom of the carbonyl group and the N(7) nitrogen atom. This bidentate behavior of guanosine has already been mentioned in such complexes with platinum [6] and palladium [7].

Acknowledgements

We are grateful to P. Braunstein, C. Morin and M. Postel for their helpful comments.

References

1 B. Rosenberg, *Naturwiss., 60,* 399 (1973) and references herein.
2 a) Lou S. Kan and Norman C. Li, *J. Am. Chem. Soc., 92,* 281 and 4823 (1970);
b) *ibid., 80,* 5069 (1968);
c) G. L. Eichhorn, P. Clark and E. D. Becker, *Biochemistry, 5,* 245 (1966);
d) Pi-Chang King and F. D. Rochon, *Can. J. Chem., 59,* (23), 3293 (1981);
e) G. Pneumatikakis, *Inorg. Chim. Acta, 66,* 131 (1982);
f) L. G. Marzilli, B. de Castro and C. Solorzano, *J. Am. Chem. Soc., 104,* 461 (1982).
3 G. L. Eichhorn and L. G. Marzilli, 'Metals Ions in Genetic Information Transfer', New York, p. 54 (1981), in *Adv. Inorg. Biochem.*
4 a) F. G. Mann, D. Crowfoot, D. Gattiker and N. Woorster, *J. Chem. Soc.,* 1642 (1935).
b) P. Spacu and D. Camboli, *Anal. Univ. Bucarest, Chimie, XIII,* No 2, 117 (1964).
5 M. Postel, M. Pfeffer and J. G. Riess, *J. Am. Chem. Soc., 104,* 461 (1982).
6 J. Dehand and J. Jordanov, *J. Chem. Soc. Chem. Comm.,* 598 (1976).
7 G. Penumatikakis, N. Hadjiliadis and T. Theophanides, *Inorg. Chem., 17,* 915 (1978).
8 E. D. Becker, H. T. Miles and R. B. Bradley, *J. Am. Chem. Soc., 87,* 5575 (1965).