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Complexes of Fe(II), Fe(III), Mn(II) and Cr(III) with 2′AMP and 3′AMP

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Mn(II), Cr(III), Fe(II) and Fe(III) derivatives with 3′AMP and 2′AMP were isolated and characterised by infrared, ultraviolet and fluorescence spectroscopy. The proximity influence of the phosphate group to the adenine ring appears to have an important role in stabilization of the metal–adenine bond.

Introduction

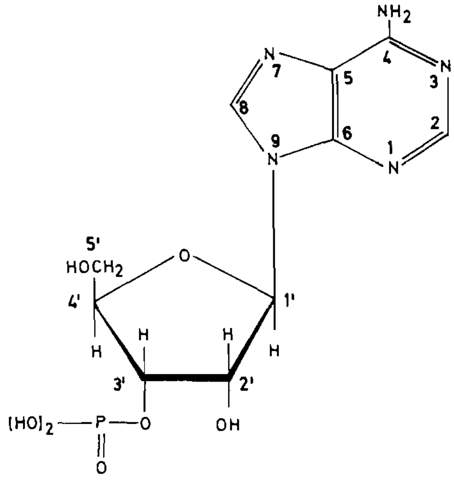
Current studies of 3d metal ions with 3′AMP and 2′AMP have been limited to investigations of solutions. Sigel [1] studied the interaction of Cu(II) with 3′AMP using ultraviolet difference spectra. Suzuki [2] observed the effects of absence of the 2′ OH group in the interaction of Co(III) with 2′AMP using circular dichroism. Heller [3] studied the interaction of Mn(II) with 2′AMP using proton NMR. The interaction of Cu(II) with 2′AMP and 3′AMP, using NMR, was studied by Berger [4]. Taqui Khan [5] determined the formation constants of the 2′AMP and 3′AMP 3d divalent cation complexes..

Our present contribution is an extension of a recently published study [6] dedicated to 5′AMP.

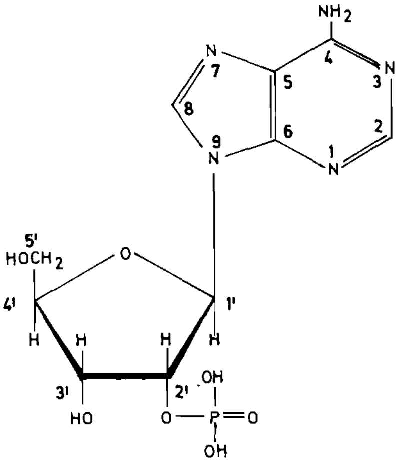
Experimental

Adenosine 3′-monophosphoric acid and adenosine 2′-monophosphoric acid (SERVA), nitrates of Fe(III), Mn(II), Cr(III) and sulphate of Fe(II) (MERCK) were used as starting products.

1 m*M* of nucleotide dissolved in 10 ml of diluted NaOH was raised to an appropriate pH to avoid precipitation of hydroxides (between 1–2 for Fe(III); 4.5 for Fe(II); 5 for Mn(II); 3 for Cr(III)). This solution was mixed with 5–10 ml of 1 m*M* solution of each metal salt. The resulting solutions were heated to 40–50 °C in a temperature controlled



$3'AMPH_2$



$2'AMPH_2$

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TABLE 1. Analytical Data for the Complexes.

Compound		Metal	C	H	N	P	μ_{eff} (B.M.)	M.P. (°C)
Mn(3'AMP)$\cdot$4H_2O	c[a]	11.64	25.41	4.24	14.83	6.57	5.56	190(d)
	f	11.84	25.37	4.26	14.36	6.51		
Cr(3'AMP)$NO_3$$\cdot$4$H_2O$	c	9.43	21.85	4.01	15.24	5.64	3.08	190(d)
	f	9.79	21.69	4.04	14.99	5.31		
Fe(3'AMP)$\cdot$4H_2O	c	11.81	25.37	4.23	14.80	6.55	4.30	190(d)
	f	11.48	25.21	4.05	14.23	6.15		
Fe(3'AMP)$NO_3$$\cdot$4$H_2O$	c	10.44	22.44	3.74	15.71	5.79	5.76	190(d)
	f	11.39	23.53	4.04	13.82	5.64		
Mn(2'AMP)$\cdot$3H_2O	c	12.10	26.42	3.96	15.41	6.83	6.09	190(d)
	f	12.32	26.45	3.97	15.15	6.10		
Cr(2'AMP)$NO_3$$\cdot$2$H_2O$	c	10.81	24.94	3.32	14.55	6.44	3.11	190(d)
	f	10.72	24.06	3.98	14.79	5.75		
Fe(2'AMP)$\cdot$3H_2O	c	12.27	26.37	3.96	15.38	6.81	4.39	190(d)
	f	11.67	26.11	4.09	14.89	6.67		
Fe_2(2'AMP)$_3$$\cdot$12$H_2O$	c	8.22	26.41	3.96	15.41	6.82	5.01	190(d)
	f	7.99	25.84	4.18	15.01	6.49		

[a] c: calcd; f: found.

bath for 1–2 hours. The complexes were precipitated by cooling or by the addition of ethanol, then they were filtered, washed with water and ethanol and dried in vacuum over P_2O_5. The Cr(III) derivatives were purified by redissolving them in a minimum amount of dilute nitric acid (1 *M*) with 0.5 m*M* of chromium nitrate added to the solution. This was heated in the bath for 1 hour and then precipitated by addition of ethanol. The complexes were stable at room temperature in the desiccator.

Carbon, hydrogen and nitrogen contents were determined by elemental analysis (at the Institute of Bio-organic Chemistry of Barcelona) using a Carlo Erba analyzer. Phosphorus was determined by the phosphomolybdovanadate method. Metals were detected by atomic absorption or spectrophotometric methods using a PERKIN ELMER 552 ultraviolet–visible spectrophotometer and a PERKIN ELMER 705 atomic absorption spectrophotometer. Infrared spectra were obtained as KBr pellets with a PERKIN ELMER 683 spectrophotometer. Magnetic susceptibility was measured (at the Institute of Applied Organic Chemistry of Barcelona) by Faraday's method. Fluorescence was measured with a double beam FICA MK II spectrophotometer.

Results and Discussion

The complexes are only slightly soluble in water (to concentrations of the order of 1×10^{-3} to 1×10^{-4}), so molecular weight determinations are not feasible. All complexes, with the exception of the Fe(III) derivative with 2'AMP, display 1:1 stoichiometry with a microcrystalline structure.

The infrared spectra bands were assigned by analogy with 5'AMP's. The most characteristic bands are those of the adenine ring in the zone 1550–1700 cm^{-1}; those of phosphate from 1250 to 950 cm^{-1} and those of phosphoric ester near 800 cm^{-1} [7–12]. The phosphoric ester band, in the zone from 800 to 740 cm^{-1} according to Dietsch, appears in the 5'-ribose phosphate as a band of medium intensity at 800 cm^{-1} and slightly shifted in 2'AMP and 3'AMP. In the case of adenine, in this zone, only weak bands are present. The data are shown in Table II for 3'AMP derivatives and in Table III for 2'AMP derivatives.

The infrared bands of nucleotides change frequencies and forms as a function of pH media. So, derivatives of Fe(III) and Cr(III) must be compared with the acid form of the nucleotides, and Fe(II) and Mn(II) derivatives with the sodium salt obtained by isolation from a solution with pH = 4.5.

In the 3'AMP derivatives the Fe(II) complex showed a slight shift from 1650 to 1645 cm^{-1} in the stretching C=N band, and also the ring band shifted by 3 cm^{-1} in the Mn(II) complex. The ring band from 1575 cm^{-1} was shifted to 1580 cm^{-1} in the Fe(II) and Mn(II) complexes. The Fe(III) and Cr(III) derivatives, differing from the complexes obtained with 5'AMP [6] exhibited an alteration of ring bands: the stretching C=N band from 1690 cm^{-1} was diminished in intensity but not shifted, and the ring bands from 1610 and 1555 cm^{-1} were shifted. The infrared data seem to indicate a metal–ring interaction in the complexes of Mn(II) and Fe(II) similar to that in 5'AMP derivatives and some interaction of Fe(III) and Cr(III) with the adenine ring may be due to a direct bond or through one water molecule of the metal ion coordination sphere.

TABLE II. Infrared Data for the 3'AMP Complexes (cm^{-1}).

	$H_2$3'AMP	Na_2(3'AMP) (pH = 4.5)	Mn(3'AMP)· $4H_2O$	Fe(3'AMP)· $4H_2O$	Cr(3'AMP)- $NO_3 \cdot 4H_2O$	Fe(3'AMP)- $NO_3 \cdot 4H_2O$
ν $-C{=}N^+$	1690vs	1690s	br.	1690s	1690s	1690s
ν $-C{=}N$	br.	1650vs	1650vs	1650vs	1650vs	1650vs
ν $-C{=}C-, C{=}N-$	1610s	1605s	1602s	1602s	1608s	1605s
ν –ring	1555m	1575m	1580m	1580m	1580m	1580m
ν $-P{=}O$	1225vs	1215vs	1210w	1210w	br.	1210w
ν $-PO_3^{2-}$ (asy)	br.	1110s	br.	br.	br.	1120s
ν $-PO_3^{2-}$ (sy.)	br.	980m	990vs	1010vs	1010vs	1010s
ν $-C-O-P$	790m	790m	800m	800m	(810m, 798m)[a]	(810m, 798m)[a]

[a] ν $-C-O-P + \nu_2(NO_3^-)$.

TABLE III. Infrared Data for the 2'AMP Complexes (cm^{-1}).

	$H_2$2'AMP	Na_2(2'AMP) (pH = 4.5)	Mn(2'AMP)· $3H_2O$	Cr(2'AMP)- $NO_3 \cdot 2H_2O$	Fe(2'AMP)· $3H_2O$	Fe_2(2'AMP)$_3$· $12H_2O$
ν $-C{=}N^+$	1690vs	1685vs	1675vs	1675vs	1690vs	1692vs
ν $-C{=}N$	br.	br.	br.	1648vs	1645vs	br.
ν $-C{=}C-, -C{=}N-$	1610s	1620s	1610s	1605s	1605s	1610s
ν –ring	1555m	1575m	1570m	br.	1575m	1575m
ν $-P{=}O$	1220vs	1220vs	1210w	1215w	1210w	1215w
ν $-PO_3^{2-}$ (asy)	1120vs	1115vs	1130vs	br.	1120vs	1100vs
ν $-PO_3^{2-}$ (sy.)	br.	980s	(1035, 1000, 985s)	1020s	1010s	1020s
ν $-C-O-P$	803m	825m	(845m, 795m)	(840w, 795m)[a]	(837w, 800m)	(840w, 800m)

[a] ν $-C-O-P + \nu_2(NO_3^-)$.

The intensity of the stretching P=O band diminished and was shifted to lower frequencies. The shift of the P=O band indicates weakening of the double bond by formation of the metal–O–P bond which implies a charge transfer from the phosphate group to the metal.

The symmetric stretching band of the phosphate group shifted toward higher frequencies for all the complexes, and appeared as a strong band, which indicates coordination with the phosphate group. The asymmetric stretching band appeared as a broad band for most complexes. The stretching C–O–P band shifted to higher frequencies and in the case of Cr(III) and Fe(III) overlapped with the nitrate bands. The nitrate group present in the trivalent derivatives showed the fundamental vibrational modes of the free nitrate (ν_3 at 1382 cm^{-1} and ν_2 overlapping with the C–O–P stretching band).

The infrared data seem to indicate interaction of the metal ion with the phosphate group from the 3'AMP for all the complexes.

For the 2'AMP derivatives (Table III) the stretching C=N band showed marked shifts for the Mn(II) and Fe(II) complexes and a slight shift for the Fe(III) complex. The ring stretching band from 1610 cm^{-1} in the acid was shifted for all the complexes except the Fe(III) complex. The ring band from 1565 cm^{-1} (acid form) and 1575 (sodium salt) shifted for all the complexes except for the Fe(II) complex.

The phosphate group bands were shifted in all cases similarly to the derivatives of 3'AMP. Splitting of the symmetric stretching band was observed in the Mn(II) complex. The Mn(II)–2'AMP complex also exhibits frequencies that do not appear in the nucleotide from 685, 560, 470 and 315 cm^{-1}. These bands can be tentatively assigned as coordination water [13] (ρ_r (685 cm^{-1}), ρ_w (565 cm^{-1})), and the others as a metal–oxygen stretching band from the phosphate group or the coordinated water. The assignment as ν M–N bands is improbable because purine ring or imidazol bands are expected to appear at frequencies between 200–300 cm^{-1} [14, 15]. The Cr(III) derivative exhibited only the fundamental vibrational modes of free nitrate (ν_3 at 1382 cm^{-1}).

TABLE IV. Spectroscopic Properties of the Complexes.

Compound	λ_{max} (UV–visible) (nm)			λ_{max} (Fluorescent data) (nm)		
$Mn(3'AMP)\cdot 4H_2O$	260		pH = 6	no fluorescence		
$Cr(3'AMP)NO_3\cdot 4H_2O$	260	295^s	pH = 3	....		
$Fe(3'AMP)\cdot 4H_2O$	260			ex: 285	em: 345, 405	pH = 6.5
$Fe(3'AMP)NO_3\cdot 4H_2O$	260			ex: 285	em: 400, 450	pH = 6.5
$Mn(2'AMP)\cdot 3H_2O$	260			ex: 310	em: 403	pH = 6.5
$Cr(2'AMP)NO_3\cdot 2H_2O$	260	300^s	pH = 2	....		
$Fe_2(2'AMP)_3\cdot 12H_2O$	260			ex: 285	em: 365	pH = 6.5

The infrared data would seem to indicate coordination of the metal with the phosphate group and possibly with the ring for all the 2'AMP derivatives. This behaviour is different from that of 5'AMP and 3'AMP derivatives. The coordination with the adenine ring may be feasible by steric phenomena. In the 2'AMP derivatives the proximity between the phosphate group and adenine ring is higher than in the other adenine nucleotides. This result is in agreement with that obtained from the fluorescent data, discussed below.

Ultraviolet and fluorescent data are tabulated in Table IV. Neither the 3'AMP nor the 2'AMP showed fluorescence except at very low pH's. Any shift of the ultraviolet band from 260 nm due to the adenine ring or fluorescent emission by excitation in the area 260–285 nm at pH values between 6–8 would indicate adenine–metal interaction [16], but no conclusion can be drawn for the absence of fluorescence.

Fluorescence cannot be measured for the Cr(III) complexes because at neutral pH they present olation phenomena. The 3'AMP derivatives with Fe(II) and Fe(III) show fluorescence and the 2'AMP complexes with Mn(II), Fe(II) and Fe(III) also show fluorescent emission. The non-fluorescence of the Mn(II)–2'AMP complex, in contradiction to the infrared data, may be due to sensitivity to ultraviolet light of the Mn(II)–adenine bond. Speca [15] recently obtained a Mn(II) complex with adenine sensitive to visible light; but the complex Mn(II)–3'AMP is stable to visible light. The fluorescence from Mn(II)–2'AMP can be explained by the stabilization that proximity of the phosphate group to the adenine ring provides for the Mn(II)–adenine bond. This complex presents a maximum of fluorescence by excitation at 310 nm which seems to indicate a strong metal–ring interaction.

Magnetic susceptibility studies are in agreement with an octahedral geometry for the 3d metals with the exception of Fe(II) and Cr(III) derivatives. The abnormally low values for these complexes may be due for the Fe(II) derivatives to a distorted octahedral symmetry or to a mixed equilibrium between two different spin states [17]; for the chromium derivatives it could be due to a magnetic exchange in a bi- or poly-nuclear structure. These results are similar to those obtained with the 5'AMP derivatives [6].

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