Adenosine Adducts with 3d Metal Perchlorates*

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I

Binding studies of metal ions to nucleic acid constituents are currently of great interest, in view of the crucial role played by metal ions at some stage of gene expression (replication, transcription and translation) or their ultimate combination with the gene product to produce an active metalloenzyme or other metal—protein complex [2]. In addition, several complexes of nucleic acid constituents, especially with platinum and other precious metal ions, show antitumor activity [2]. These laboratories have studied in the past the complexes formed by interaction of 3d metal perchlorates with purine [3] and some biologically important purine derivatives, such as adenine [4] and guanine [5], and more recently extended their work to include the corresponding metal complexes with adenosine (ado; I), which are the subject of the present letter. Several ado metal complexes were previously reported; among these studies, a paper dealing with $M(ado)_nCl_2$ (n = 1 or 2; M = Co, Ni, Cu, Zn, Cd, Hg) complexes [6] is the closest to the work herein reported. A number of crystal structure determinations of metal complexes with adenine nucleosides, 9-substituted adenines and nucleosides of other purines have been reported. Thus, 2'-deoxy-adenosine (dado) acts as unidentate N(7)-bonded in $[Co(dado)(acac)_2(NO_2)]\cdot 2H_2O$ (acac = acetylacetonato ligand) [7]. Guanosine also exhibits the tendency to bind through N(7) in several metal complexes [8—10], while 9-methyladenine functions as bidentate bridging N(1),N(7)-bonded in its 1:1 complex with $CoCl_2$ [11]. A most unusual case of ado chelating through the O(2') and O(3') ribose oxygens was established for the complex of this ligand with OsO_3-(pyridine)$_2$, which does not contain any N-bonded ado [12].

The synthetic procedure employed was similar to that previously used for the preparation of adenine or guanine complexes with 3d metal perchlorates [4, 5], *viz.*: treatment of 0.8 mmol of the hydrated metal
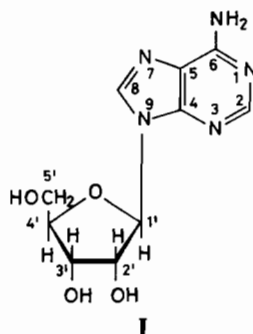
perchlorate with 50 ml of a 7:3 (v/v) mixture of ethanol and triethyl orthoformate at 50 °C for 1 h, followed by addition of 1.6 (for M^{2+}) or 2.4 (for M^{3+}) mmol ado and refluxing of the resultant mixture for 5—10 days (depending on the rate of precipitation of the complex). The refluxive step was followed by reduction of the volume of the supernatant to about one-half its original volume, separation of the solid complex by filtration, washing with ethanol—triethyl orthoformate and storage *in vacuo* over anhydrous $CaCl_2$. The new complexes isolated are adducts of the types: $M_2(ado)_3(ClO_4)_6\cdot 4H_2O$ (M = Cr, Fe), $M(ado)(ClO_4)_2\cdot 2H_2O$ (M = Mn, Co, Ni, Cu) and $M(ado)(ClO_4)_2$ (M = Fe, Zn). The complexes are generally characterized by insolubility or very poor solubility in organic media. Characterization work, currently in progress, is based on spectral and magnetic studies.

The ν_{NH_2} bands of free ado at 3330, 3160 cm^{-1} [13—15] appear intact in the spectra of the two water-free complexes, but are partially or completely masked by the ν_{OH} band [16] in the spectra of the hydrated species. The δ_{NH_2} band of ado at 1667 cm^{-1} [13—15] does not undergo significant shifts upon 3d metal perchlorate adduct formation, so that it can be concluded that the ligand does not coordinate through the nitrogen of the exocyclic NH_2 group at C(6) [4, 13—15]. The ν_3 mode of ionic ClO_4^- appears as a single band only when M = Cu^{2+} (1090 cm^{-1}), while in the rest of the complexes it is triply split (maxima at 1122—1114, 1100—1075 and 1065—1049 cm^{-1}), indicating that both ionic ClO_4^- and coordinated $-OClO_3$ are present in these species [17]. Coordination of ado through ring nitrogens is suggested by shifts and frequent splittings of the $\nu_{C=C}$, $\nu_{C=N}$ and ring vibrational modes of the free ligand at 1650—1300 cm^{-1} (1650, 1603, 1570, 1468, 1310) upon adduct formation [4, 13—15], and the identification of ν_{M-N} absorptions in the lower frequency IR region (Table I). Regarding the possibility of coordination of ado through hydroxyl oxygens of the sugar moiety, the free ligand exhibits a number of additional bands, relative to adenine, at 371, 309, 295 and 263 cm^{-1}; these bands are probably due to

TABLE I. Tentative $\nu_{M-Ligand}$ Band Assignments for the New ado Metal Complexes (cm^{-1}).

M^{n+}	ν_{M-O}(aqua)	ν_{M-O}($-OClO_3$)	ν_{M-N}
Cr^{3+}	500m	330m	290mb
Mn^{2+}	426m	329m	251w,246w
Fe^{2+}		348m	303w,295w
Fe^{3+}	490m	326mb	285mb
Co^{2+}	450m	340m	278w,262w
Ni^{2+}	454m	342m	280w,265w
Cu^{2+}	475ms		314w,299w
Zn^{2+}		338m	285w,271w

sugar moieties [18]. They undergo little changes in the spectra of the hydrated new complexes, but in those of the water-free compounds (M = Fe^{2+}, Zn^{2+}) the 295 cm^{-1} band is not observed, and the rest of these bands show relatively larger shifts. The two water-free complexes might, thus, involve direct interaction of the metal ions with one or more of the ribose hydroxyl groups [12, 18].

The coordination numbers suggested by the tentative $\nu_{M-ligand}$ band assignments of Table I are four for M = Fe^{2+}, Cu^{2+}, Zn^{2+}, five for M = Mn^{2+}, Co^{2+}, Ni^{2+} and six for M = Cr^{3+}, Fe^{3+} [3–6, 16, 19–20]. Similar conclusions are drawn from the d–d transition spectra of the complexes, *i.e.*: distorted tetrahedral symmetry for the Fe^{2+} and Cu^{2+} adducts [6, 21–23], which show the following maxima, nm: Fe^{2+}: 503m, 588mw, 901mw, 702m, 750mb, 977wb; Cu^{2+}: 572m,sh, 618ms,b, 770s,vb; coordination number five for the Co^{2+} and Ni^{2+} complexes, which exhibit multiple d–d band maxima at 350–1300 nm [20, 24, 25], *viz.*: Co^{2+}: 477s,sh, 496s, 522s,sh, 620w, b, 715w,vb, 833wb, 917wb, 1050w,vb, 1260wb; Ni^{2+}: 385s, 421ms, 445ms,sh, 497m,sh, 590mw,b, 671mw,b, 740mw,b, 975w,b, 1260wb; and a low symmetry hexacoordinated configuration for the Cr^{3+} complex [5, 24], which shows split d–d bands, nm: 422s, 447s, 491m,sh, 540mw,sh, 571wb, 629wb, 690w,vb (approximate D_q = 1587 cm^{-1}).

The evidence so far available, combined with the poor solubility of the new complexes in organic media and the pronounced tendency of purines to function as bridging ligands [26], is in favor of polymeric structures for these compounds; in addition, the fact that the M^{3+} complexes involve 3:2 ado to metal ion molar ratios is also in support of non-monomeric configurations. For the hydrated M^{2+} complexes (M = Mn, Co, Ni, Cu), structural types involving a single-bridged linear chainlike polymeric backbone, *i.e.* $\{M-ado\}_n$, with terminal aqua ligands for M = Cu, and both aqua and $-OClO_3$ ligands for M = Mn, Co, Ni, would seem most likely for the cationic species [3–5, 20, 21, 27] (anionic ClO_4^- is also present). As regards the M^{3+} complexes, two alternatives exist for the polymeric cationic

complexes: a similar one to the preceding single-bridged linear chainlike polymeric backbone with terminal aqua, $-OClO_3$ and unidentate ado ligands, and a structural type involving a polymeric backbone with alternating single and double ado bridges between adjacent metal ions, *i.e.*, $\{M-ado-M-(ado)_2\}_n$, and terminal aqua and $-OClO_3$ ligands. Unidentate ado, if present in the M^{3+} complexes, would certainly coordinate through N(7) [7–10], while bidentate bridging ado would use N(1) and N(7) as its binding sites [11] (coordination of ado through N(3) would be probably sterically hindered, owing to the proximity of the ribose substituent at N(9) [28]. In the case of the water-free M^{2+} complexes (M = Fe, Zn), coordination number four would be attained by use of N(1), N(7) and one of the ribose hydroxyl oxygens (O(2') or O(3')) of ado in binding to the metal ions [3–5, 11, 12, 18, 20, 21, 29]. Structural type **II**, which involves cross-linking of two linear $\{M-ado\}_n$ polymeric units via OH oxygens of the ligand, is considered as likely (L–OH: tridentate N(1), N(7), O-bonded ado; X = $-OClO_3$ ligand). A full account of the work herein presented will be published upon completion of our characterization studies.

$$\left[\begin{array}{c} X \\ | \\ -M- \\ | \\ OH \\ | \\ -L- \end{array} \quad \begin{array}{c} \\ \\ -L- \\ | \\ OH \\ | \\ -M- \\ | \\ X \end{array} \right]_n (ClO_4)_{2n}$$

II
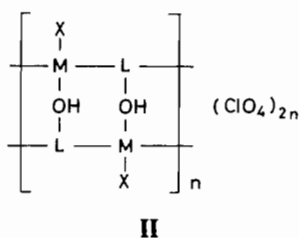
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