Chelates of Tetracycline with First Row Transition Metal Perchlorates

CHESTER M. MIKULSKI, JAMES FLEMING, DEBORAH FLEMING

Department of Chemistry & Physics, Beaver College, Glenside, Pa. 19038, U.S.A.

and NICHOLAS M. KARAYANNIS

*Amoco Chemical Co., P.O. Box 400, Naperville, Ill. 60566, U.S.A.*

(Received June 3, 1987)

Abstract

2:1 adducts of tetracycline (tc) with 3d metal perchlorates ($M = Cr^{3+}$, Mn^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}) are synthesized by boiling under reflux mixtures of tc free base and metal salt in ethanol–triethyl orthoformate. Characterization studies suggest that the new complexes are monomeric chelates involving bidentate tetracycline ligands, chelating via the amide group oxygen and the C3–O oxygen of the ring A tricarbonylmethane. The complexes also contain unidentate coordinated $-OClO_3$ ligands, as well as ionic ClO_4^-. The M^{3+} (Cr, Fe) complexes are hexacoordinated of the $[M(tc)_2(OClO_3)_2]ClO_4$ type (MO_6 chromophores), with two bidentate chelating tc and two unidentate perchlorato ligands in the first coordination sphere of the central metal ion. In the M^{2+} (Mn, Fe, Co, Ni, Cu, Zn) complexes, the inner coordination sphere of the metal ion is occupied by two bidentate chelating tc and only one $-OClO_3$ ligand, and the coordination number is five, *i.e.* $[M(tc)_2OClO_3]ClO_4$ (MO_5 absorbing species).

Introduction

The syntheses of 3d metal perchlorate adducts with tetracycline (tc; **I**) were recently reported by these laboratories in a number of preliminary communications [1, 2]. The metal complexes of tc and its derivatives have attracted attention in view of the fact that some of the biological effects of these antibiotics arise from their interactions with metal ions [3–5]. The affinity of tetracyclines for metal ions is well documented [3–12]. Studies involving formation of tetracycline metal complexes in solution have been most frequently carried out [3–9], but a number of solid complexes have been also isolated and characterized, including Co^{2+}, Ni^{2+} [10, 11] and Ca^{2+} [12] complexes with anionic tc^- of the $M(tc^-)_2$-$(OH_2)_2$ type [10–12]. The latter complexes were precipitated from methanol solutions of tetracycline hydrochloride and MCl_2 (M = Co, Ni, Ca), after

I
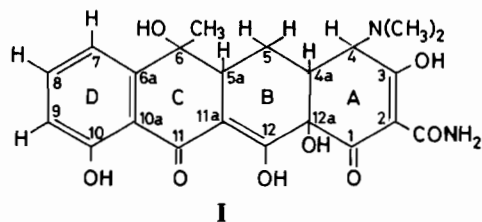
adjusting the pH of the combined mixture to 7.4 by adding triethylamine [10–12]. In our recent synthetic work we were able to prepare water-free adducts of tc with 3d metal perchlorates ($M^{n+} = Cr^{3+}$, Mn^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}) [1, 2], by employing a synthetic method similar to that used for the syntheses of metal perchlorate adducts with purine [13]. The present paper deals with our preparative and characterization studies of these adducts.

Experimental

Reagent grade tetracycline free base (Fluka) and hydrated metal perchlorates (G.F. Smith Chemical Co.) were used without any further purification. The synthetic method employed was as follows [2]: 1.4 mmol hydrated metal salt are dissolved in a mixture of 35 ml absolute ethanol and 15 ml triethyl orthoformate (teof), at 40–50 °C. Then, 2.5 mmol tc are added to the warm solution and the resultant mixture is boiled under reflux for 24–48 h. Subsequently, the volume of the mixture is reduced by about 50%, by heating under reduced pressure, and the residue is allowed to cool to room temperature. The precipitated complex is separated by filtration, washed with cold absolute ethanol and stored *in vacuo* over anhydrous $CaCl_2$. With one exception ($M = Cu^{2+}$), this procedure resulted in the formation of 2:1 adducts of tc with the metal perchlorate, *i.e.* $M(tc)_2$-$(ClO_4)_3$ (M = Cr, Fe) and $M(tc)_2(ClO_4)_2$ (M = Mn, Fe, Co, Ni, Cu, Zn). The interaction of tc with $Cu(ClO_4)_2$ under the above conditions led to the precipitation of

TABLE I. Analytical Data for the tc Metal Complexes

Complex[a]	Yield (%)	Found (calc.) (%)				
		C	H	N	M	Cl
$Cr(tc)_2(ClO_4)_3$	95	43.1(42.8)	4.0(3.9)	4.7(4.5)	4.1(4.2)	8.7(8.6)
$Mn(tc)_2(ClO_4)_2$	42	46.8(46.4)	3.8(4.2)	5.1(4.9)	4.6(4.8)	6.5(6.2)
$Fe(tc)_2(ClO_4)_2$	82	46.1(46.4)	3.9(4.2)	4.6(4.9)	5.1(4.9)	6.6(6.2)
$Fe(tc)_2(ClO_4)_3$	92	43.0(42.7)	3.9(3.9)	4.1(4.5)	4.8(4.5)	8.3(8.6)
$Co(tc)_2(ClO_4)_2$	66	45.9(46.2)	4.0(4.2)	4.6(4.9)	5.2(5.2)	6.1(6.2)
$Ni(tc)_2(ClO_4)_2$	77	46.7(46.3)	3.9(4.2)	4.8(4.9)	5.4(5.1)	6.0(6.2)
$Cu(tc)_2(ClO_4)_2$	91	45.7(46.1)	3.8(4.2)	4.7(4.9)	5.2(5.5)	6.5(6.2)
$Zn(tc)_2(ClO_4)_2$	28	45.7(46.0)	4.1(4.2)	5.1(4.9)	6.1(5.7)	6.4(6.2)
$tcH^+ClO_4^-$	93	49.0(48.7)	4.6(4.6)	5.0(5.2)	[b]	6.3(6.5)

[a]The complexes are generally brown in color, ranging from very dark (almost black: Cr^{3+}, Cu^{2+}) to medium (Mn^{2+}, Fe^{3+}, Ni^{2+}) to light (Fe^{2+}, Co^{2+}, Zn^{2+}) shades of brown. [b]Cu content of the perchlorate salt of tc was determined to be <0.2% (see 'Experimental').

the $HClO_4$ complex of tc ($tcH^+ClO_4^-$). We were able to prepare $Cu(tc)_2(ClO_4)_2$ by briefly heating a 2:1 molar solution of tc and Cu^{2+} salt at 60 °C, under stirring, and then allowing the mixture to stand at ambient temperature for 1–2 days. The precipitate formed was treated and stored as described above. Table I gives analytical data (Schwarzkopf Microanalytical Laboratory, Woodside, N.Y.). Solubility studies indicated that the complexes are insoluble in ethanol, diethyl ether or water; most of the complexes are also insoluble in nitromethane or acetone, but those with Fe^{2+}, Fe^{3+} and Cu^{2+} show limited solubility in these media. The $tcH^+ClO_4^-$ salt is soluble in various organic solvents, including ethanol, nitromethane and acetone.

Characterization of the new complexes was based on spectroscopic, magnetic and conductance studies. IR spectra (Tables II–IV) were recorded on KBr discs (4000–500 cm^{-1}) and Nujol mulls between NaCl (4000–700 cm^{-1}) and high-density polyethylene (700–200 cm^{-1}) windows, using a Perkin-Elmer 621 spectrophotometer. Solid-state electronic spectra (Table V) were obtained on Nujol mulls of the complexes, applied on thin tissue paper [14], using a Cary model 14 spectrophotometer. Magnetic susceptibility measurements at 300 K (Table V) were performed as described elsewhere [14]. Molar conductivities were determined on 10^{-3} M solutions of the complexes in 1:1 (v/v) nitromethane–acetone at 25 °C, using a Yellow Springs Instrument Co., Model 31 conductivity bridge and a cell calibrated with a 10^{-3} M tetra-n-butylammonium perchlorate solution in the same solvent mixture ($\Lambda_M = 97$ Ω^{-1} cm^2 mol^{-1}) [15, 16]. The Λ_M values obtained (M = Fe^{2+} 71; M = Fe^{3+} 77; M = Cu^{2+} 69; and $tcH^+ClO_4^-$ 91 Ω^{-1} cm^2 mol^{-1}) correspond to uni-univalent electrolytes [17].

Results and Discussion

The general trend observed during this synthetic study was the formation of 2:1 adducts of neutral tc with the 3d metal perchlorates. As already mentioned, monoanionic tc^- also produced 2:1 complexes with the Co^{2+}, Ni^{2+} and Ca^{2+} ions [10–12]. Therapeutically active tetracyclines form 2:1 complexes with various metal ions, while certain therapeutically inactive derivatives yield only 1:1 complexes with the same metal ions [7]. The formation of $tcH^+ClO_4^-$, instead of the $Cu(ClO_4)_2$ adduct, upon refluxing a mixture of tc and the Cu^{2+} salt in ethanol–teof, is not unprecedented. In fact, the isolation of $L_nH^+ClO_4^-$ salts ($n = 1, 2$) during reactions between neutral ligands and metal perchlorates has been reported on several occasions, e.g. L = 2,6-lutidine N-oxide [18], phenazine 5-oxide [19] and triphenylphosphine oxide [20]. The repeatability of $tcH^+ClO_4^-$ precipitation during the above reaction was confirmed by performing the experiment twice. Since the complete IR spectrum of tcH^+Cl^- has been reported [21] and compared to the spectra of $M(tc^-)_2(OH_2)_2$ complexes [11], it was felt that comparisons of the spectra of tc free base, tcH^+Cl^- and $tcH^+ClO_4^-$ were in order, and selected IR maxima of these three compounds are given in Table II, in which the components of the amide I–V bands assigned by Dzięgielewski *et al.* [21] were identified on the basis of pertinent literature assignments [22]. The spectra of the three compounds are virtually identical in most regions. However, there are noticeable differences between the spectra of the free base and the two tcH^+X^- (X = Cl, ClO_4) salts in the amide I–V regions. This is due to the fact that the free base exists in the non-ionized form I in the crystal and non-aqueous media (adopting a zwitterionic state

TABLE II. Selected Maxima in the IR Spectra (4000–600 cm^{-1}) of tcH$^+$Cl$^-$, tc Free Base and tcH$^+$ClO$_4^-$

tcH$^+$Cl$^-$ [a]	tc free base	tcH$^+$ClO$_4^-$	Band assignment[b, c]
3609m	3616m	3611m	ν(OH)
3361s	3360s	3358s	ν_{as}(NH$_2$)
3300s	3300s	3295s	ν_s(NH$_2$)
3104m, 3087m, 3060m,	3110m, 3082m, 3060m,	3106m, 3090m, 3063m,	} ν_{as}(CH$_3$) + ν(CH)(skeleton) + ν_s(CH$_3$)
2985m, 2944m, 2930w	2985m, 2945m, 2928w	2980m, 2940m, 2925w	
	1770w,b	1760vw,vb	d
1670vs	1663s, 1644s	1670vs	Amide I (ν(C=O) + δ(NH$_2$))
1638m	1638m	1640m	ν(CC) naphthacene skeleton
1611vs	1611vs	1610vs	ν(C=O) ring A
1580vs	1575vs	1577vs	ν(C=O) ring C
1560sh	1560sh	1558sh	ν(CC)
1520s	1515s	1523s	Amide II (δ(NH$_2$) + ν(C–NH$_2$))
1450s, 1414w,	1448s, 1429sh,	1450s, 1417w,	} δ(COH) + δ(CH$_3$)
1376s, 1356s	1391m, 1367m	1381s, 1360ms	
1247s, 1226vs	1244sh, 1220s	1246s, 1232s	Amide III (δ(NH$_2$) + ν(C–NH$_2$) + ν(C2–C=O))
1175m, 1156w, 1139s,	1170m, 1158m, 1147sh,	1173s, 1134vs,sh, [e]	} ν(C–O) + ν(CC) + ν(C–N) + β(CH)
1132sh, 1111s	1120m, 1108m		
		1090vvs	ν_3(ClO$_4$)
938m	941m	943m	β(CH)
693vs,b	688s,b	695s,b	Amide V (γ(NH$_2$))
669s	657s	672s	Amide IV (δ(C–NH$_2$) + δ(C=C–N))
650m, 632m	650m, 631m	648m, [e]	δ(C–C(=O)–C) + γ(OH)
		619svs	ν_4(ClO$_4$)

[a] Assignments from ref. 21. [b] Based on the assignments of Dzięgielewski *et al.* for the tcH$^+$Cl$^-$ [21] and ref. 28 for the ClO$_4^-$ bands. [c] The components of the Amide I–V were assigned on the basis of ref. 22. [d] Absorption in this region was not reported for tcH$^+$Cl$^-$ [21]; this band is probably due to combination modes. [e] Masked by ClO$_4$ bands.

with both charged sites on ring A in its hydrates or in aqueous media) [3, 21, 23–25], whereas in tc hydrochloride and, presumably, the perchlorate salt, the double bond of ring A is delocalized and the acidic hydrogen atom is attached to the oxygen atom of the amide group; the ionic character of the –C(OH)= NH$_2$ group thus produced is compensated by the X$^-$ anion [3, 21, 24–27]. Thus, while the tcH$^+$X$^-$ salts exhibit a single band at 1670 cm^{-1} in the amide I region (ν(C=O) + δ(NH$_2$)), the free base shows a doublet at 1663 and 1644 cm^{-1}. In the amide II–V regions, the general trend is the occurrence of the bands in the spectrum of the free base at lower wavenumbers relative to the corresponding bands in the spectra of the tcH$^+$X$^-$ salts. Some differences between the spectra of the free base and its salts are also observed in the δ(OH) + δ(CH$_3$) region (1450–1350 cm^{-1}). It is also of interest to note that, whereas Dzięgielewski *et al.* did not observe a weak absorption at about 1770 cm^{-1} in the spectrum of tcH$^+$Cl$^-$ [21], our IR studies establish the presence of such an absorption in the spectra of both the free base and the perchlorate salt. This is significant, because a weak band at 1770–1760 cm^{-1} in the spectra of M(tc$^-$)$_2$(OH$_2$)$_2$ (M = Co, Ni) was assigned as a C3–O–metal vibrational mode, by comparison to the available spectrum of tcH$^+$Cl$^-$ [11]. Since this band is present in the spectra of both tc free base and

tcH$^+$ClO$_4^-$, it obviously arises from combination modes of the ligand. Finally, the perchlorate salt exhibits the characteristic ν_3 and ν_4(ClO$_4$) vibrations at 1090 and 619 cm^{-1}, respectively [28].

Relevant IR spectral data for the new metal complexes are given in Tables III (4000–600 cm^{-1}) and IV (500–230 cm^{-1}), along with the corresponding spectra of tc free base. The spectra of the complexes are devoid of ν(OH) bands attributable to coordinated water or ethanol. Metal complex formation does not appreciably affect the ligand ν(OH) and ν_s(NH$_2$) bands, but causes significant shifts of ν_{as}(NH$_2$) to higher wavenumbers (from 3360 to 3416–3385 cm^{-1}). This indicates that the NH$_2$ nitrogen of the amide group is not involved in coordination [29]. On the other hand, the amide I region (ν(C=O) + δ(NH$_2$)) bands of the ligand are shifted to lower frequencies in the spectra of the metal complexes, while the amide III main ligand band at 1220 cm^{-1} undergoes small positive frequency shifts. These trends are consistent with participation of the C=O oxygen of the amide group in coordination [11, 29, 30]. The amide II absorption of the ligand (1515 cm^{-1}) is split into two components in the spectra of the complexes, whilst the amide IV and V bands undergo small shifts upon complex formation. The ν(C=O) bands corresponding to carbonyl oxygens attached to the ring C1 and C11 carbons (1611 and

TABLE III. Relevant IR Data for tc Complexes with Metal Perchlorates (4000–600 cm^{-1})

tc[a]	M = Cr^{3+}	M = Mn^{2+}	M = Fe^{2+}	M = Fe^{3+}	M = Co^{2+}	M = Ni^{2+}	M = Cu^{2+}	M = Zn^{2+}	Band assignment[b]
3616m	3605m	3611m	3617m	3603m	3610m	3610m	3609m	3607m	ν(OH)
3360s	3412vs	3390vs,b	3415vs	3385vs	3417vs	3405vs	3395vs	3416vs	νas(NH2)
3300s	3310s	3305s	3312s	3295s	3310s	3307s	3302s	3312s	ν$_s$(NH$_2$) b
1770w,b	1765w,b	1775w,b	1760vw	1745w	1770w,b	1760vw	1775w	1764w	Amide I (ν(C=O) + δ(NH$_2$))
1663s, 1644s	1647s,sh	1645s,sh	1644s,sh	1645s,sh	1650s,sh	1648s,sh	1651s,sh	1650s,sh	ν(CC) naphthacene skel.
1638m	1638s,sh	1639s,sh	1636vs	1639s,sh	1631s,sh	1637vs	1641s,sh	1640s,sh	ν(C=O) ring A
1611vs	1622vs	1613vs	1618vs	1613vs	1600vs,vb	1606vs	1617vs	1607vs,b	ν(C=C) ring C
1575vs	1569vs	1580vs	1575vs	1564vs		1585vs	1569vs	1572vs	
1515s	1530s, 1488s	1528s, 1490s	1532s, 1479s	1526s, 1475s	1542ms, 1492s	1536m, 1486s	1523s, 1480s	1529s, 1477s	Amide II (δ(NH$_2$) + ν(C–NH$_2$))
1448s, 1429sh,	1455s, 1425sh,	1448s, 1435sh,	1447s, 1433sh,	1441s, 1420sh,	1460s, 1418sh,	1464s, 1422w,	1449s, 1424sh,	1451s, 1429sh,	
1391m, 1367m	1399m, 1375m	1380m,b	1392m, 1371m	1369m,b	1400m, 1378m	1403m, 1377m	1402m, 1390m, 1366m	1403m, 1390m, 1387m,b	δ(COH) + δ(CH$_3$)
1244sh, 1220s	1234s	1231ms	1224s	1223s	1230s	1231s	1233s	1224s	Amide III (δ(NH$_2$) + ν(C–NH$_2$) + ν(C2–C=O))
1170m, 1158m, 1147sh, 1108m	1175w, 1136m, 1150m,sh	1173w, 1150m,sh	1168w	1180w, 1145m,sh	1170w, 1145m,sh	1170w, 1130ms	1171w, 1128ms	1170w, 1140w, 1125m,sh	ν(C–O) + ν(CC) + ν(C–N) + β(CH))[c]
	1113vs, 1095vvs, 1050vs,sh	1118vs, 1090vvs, 1045vs,sh	1111vs, 1085vvs, 1052vs,sh	1120vs, 1075vvs, 1050s,sh	1118vs, 1085vvs, 1055vs,sh	1110vs, 1085vvs, 1060s,sh	1107vs, 1078vvs, 1055s,sh	1109vs, 1088vvs, 1060vvs,sh	ν$_3$(ClO$_4$)
938m	927m	921m	921m	920m	919m	922m	936w, 926m	927m	β(CH) + ν(ClO$_4$)
688s,b	696w	690vw	697w	690w	697w	696w	689m	690w	Amide V (γ(NH$_2$))
657s	662w	662w	670w	661w,b	666w	663m	670m	660mw	Amide IV (δ(C–NH$_2$) + δ(O=C–N))
	650s, 626s, 613	665w, 662m, 616m	646m, 621s, 612s	645s, 621s, 613s	645ms, 620s, 610s	651m, 622s, 617s	648s, 619s, 611s	650m, 622s, 614s	ν$_4$(ClO$_4$)

[a]Free base.   [b]See Table II.   [c]The 1108 cm^{-1} tc band is masked by the ν$_3$(ClO$_4$) band in the spectra of the adducts.

TABLE IV. Tentative Metal–Ligand Band Assignments for the New tc Complexes (500–250 cm^{-1})

M^{n+}	$\nu(M-O-C3)$	$\nu(M-OClO_3)$	$\nu(M-O=CNH_2)$	tc bands + $\nu_2(ClO_4)$ [a, b]
Cr^{3+}	444m	333w	300w	490m, 460m, 370w,b, 244w
Mn^{2+}	402w, 391w	309w	252w	490m, 460m, 377w, 340w, 240w,sh
Fe^{2+}	407w, 390w	313w	253w	490m, 450m,b, 380w,b, 345w, 240w,sh
Fe^{3+}	435w,b	328w	295w	500w,b, 450w,b, 375w, 345w, 242w
Co^{2+}	414w, 388w	316w	259w	485m, 460w, 370w, 345w, 235w
Ni^{2+}	421w, 390w	319w	268w	490m, 460m, 372w, 350w,b, 237w
Cu^{2+}	427w, 396w	322w	273w	485m, 450m,b, 375w, 350w,sh, 240w
Zn^{2+}	400w,b	311w	248w	490m, 450m,b, 378w, 345w

[a]Free tc bands in the region, cm^{-1}: 488s, 456m, 441m, 378m, 356sh, 339w, 327w, 242w [21].   [b]The IR-active $\nu_2(ClO_4)$ bands of the coordinated $-OClO_3$ ligands [28, 32] are masked by the more intense tc absorptions at 500–450 cm^{-1}.

TABLE V. Solid-state (Nujol mull) Electronic Spectra and Magnetic Properties (300 K) of the New tc Complexes

Complex	λ_{max} (nm)[a]	$10^6 \times \chi_M^{cor}$ (cgsu)	μ_{eff} (μ_B)
$Cr(tc)_2(ClO_4)_3$	208vvs, 278vs,vb, 345vs, 370s, 450s,b, 545ms, 630m, 685m	6162	3.86
$Mn(tc)_2(ClO_4)_2$	214vvs, 282vvs, 367vs, 455s,b, 522m,sh, 567w,b	14582	5.94
$Fe(tc)_2(ClO_4)_2$	212vvs, 250vs,b, 270vs, 310vs, 366s, 475m, 700mw,b, 805mw,b, 940w,b, 1380w,vb	10863	5.13
$Fe(tc)_2(ClO_4)_3$	211vvs, 274vvs,b, 369s, 465s,sh, 511m,sh, 540w,b, 603vw,b	15911	6.20
$Co(tc)_2(ClO_4)_2$	212vvs, 246vs,b, 273vs, 294vvs, 369s, 455m,b, 507m,sh, 620w, 705w,b, 810w,b, 965w, 1375w,b, 1875vw,b	8961	4.66
$Ni(tc)_2(ClO_4)_2$	209vs, 242s,b, 271vvs, 294vvs,b, 367s, 428s,b, 560m,sh, 630m, sh, 718w,sh, 835w,sh, 977w, 1280w,b, 1860vw,b	4814	3.41
$Cu(tc)_2(ClO_4)_2$	208vs, 237vs,b, 280vvs,b, 372svs, 503vs, 548vs,b, 650s,vb, 920w,vb	1555	1.94
$Zn(tc)_2(ClO_4)_2$	218vs, 265vvs, 372vvs,b, 404vs,sh, 501w,sh	diamagnetic	

[a]UV solution spectrum of tc at pH 7.58: λ_{max} (nm) (ϵ): 220 (12500), 271 (17300), 360 (13400) [12]. Nujol mull spectrum of tc free base (this work) (nm): 222vs, 271vvs, 362vs.

1575 cm^{-1}, respectively [21]), are not very sensitive to metal complex formation, undergoing small shifts in either direction. Hence, coordination of tc through these oxygen sites is ruled out [11]. In all previous studies, the function of tc as a bidentate chelating agent, binding through a variety of sites, was proposed as follows: O,O-bound tc, coordinating through the oxygens attached at (C2)C, C3 [10, 11, 25, 31], (C2)C, C1 [10, 25, 31], C1, C12 [8], C10, C11 [8], C11, C12 [8, 12] or C12, C12a [31]; and O,N-bound tc, coordinating through the oxygen at C3 or C12a and the nitrogen at C4 [7]. Since the complexes herein reported involve coordination of tc via the C=O oxygen of the amide group, while the oxygen at C1 is not participating in binding, it follows that the second binding site of the chelating ligand is the oxygen at C3, as is also the case with other tetracycline metal complexes [10, 11, 31]. The ligand bands at 1170–1100 cm^{-1} involve $\nu(C-O)$ contributions [21], but their response to metal complex formation cannot be detected, owing to the interference of the very strong $\nu_3(ClO_4)$ bands in this region [28, 32]. The perchlorate groups present in the new complexes are clearly of two types, namely ionic ClO_4^- and unidentate coordinated $-OClO_3$ ligands. This is indicated by the fact that both ν_3 and $\nu_4(ClO_4)$ are triply split and $\nu_1(ClO_4)$ is IR-active (the $\nu_2(ClO_4)$ absorption region is masked by ligand bands) [28, 32], and is also substantiated by the behavior of the soluble Fe^{2+}, Fe^{3+} and Cu^{2+} complexes as 1:1 electrolytes in nitromethane–acetone [17] (see 'Experimental'). Finally, a weak band at 1775–1745 cm^{-1} is invariably present in the spectra of the complexes; this band is presumably due to combination modes originating from tc (*vide supra*).

Tentative $\nu(M-O)$ band assignments at 450–240 cm^{-1} (Table IV) are consistent with the presence of tc ligands binding via C=O and C–O oxygens, as well as perchlorato ligands [33–39]. Thus, the $\nu(M-O)$ bands at 444–435 for M^{3+} and 427–388 cm^{-1} for M^{2+} complexes are in the region where ROH adducts [33] or RC$^-$ complexes [34, 35] with 3d metal ions exhibit their M–O stretching modes. The $\nu(M-O)$-$(OClO_3)$ bands at 333–328 (M^{3+}) and 322–309 (M^{2+}) cm^{-1} [36] are indicative of coordination numbers six for the M^{3+} and five for the M^{2+} com-

plexes [37]. The $\nu(M-O=CNH_2)$ absorptions were identified at 300–295 (M^{3+}) and 273–248 (M^{2+}) cm^{-1} [38, 39]. The $\nu(M-O)(C-O)$ and $\nu(M-O)$-$(C=O)$ band assignments are also compatible with the coordination numbers suggested by the $\nu(M-O)$-$(OClO_3)$ bands [33–35, 38, 39].

The magnetic moments of the new complexes at 300 K (Table V) are normal for high-spin $3d^3-3d^8$ compounds or the $3d^9$ configuration [40]. Moreover, the μ_{eff} values of the Co^{2+} and Ni^{2+} complexes (4.66 and 3.41 μ_B, respectively) are within the range corresponding to pentacoordinated complexes of these metal ions [37, 41–43]. The UV spectrum of tc is characterized by three main maxima at 220–360 nm [12, 44] (220, 271 and 360 nm in solution at pH 7.58 [12]; 222, 271, 362 nm in Nujol mull). These maxima appear at 208–218, 265–282 and 366–372 nm in the spectra of the new complexes (Table V). Occacional splittings of these bands were observed, as follows: the Fe^{2+}, Co^{2+} and Ni^{2+} complexes exhibit additional maxima at 242–250 and 294–310 nm, the Cu^{2+} complex shows a maximum at 237 nm and the Cr^{3+} adduct a band at 345 nm. It should be mentioned that solution UV studies of tc in various media (at pH 7.58, in 0.1 N HCl or in acetate buffer of pH 5.0) have revealed the occurrence of distinct peaks or shoulders at 240–250 and *ca.* 320 and 340 nm [12, 44]. Strong charge-transfer absorption extending to *ca.* 550 nm is invariably observed in the spectra of the complexes. The d–d transition spectrum of the Cr^{3+} complex is compatible with a low symmetry hexacoordinated configuration [45], *i.e.* nm: $^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ 450; $\rightarrow {}^4T_{2g}(F)$ 545, 630, 685. The approximate Dq value calculated is 1613 cm^{-1}. The d–d transition spectra of the M^{2+} complexes are consistent with coordination number five [45–48], *viz.* nm: M = Fe^{2+} 700, 805, 940, 1380; Co^{2+} 455, 507, 620, 705, 810, 965, 1375, 1875; Ni^{2+} 482, 560, 630, 718, 835, 977, 1280, 1860; Cu^{2+} 503, 548, 650, 920.

The evidence discussed is in favor of the presence of tc ligands binding through oxygen sites to the metal ions. The most likely case is that tc is bidentate chelating, binding through the amide group and C3 oxygens, and the complexes are monomeric. It should be noted, however, that the possibility of function of tc as bridging quadridentate, by chelating via the C1 or C3 and the amide group oxygens to one metal ion and the C12 and C12a oxygens to an adjacent metal ion, has been demonstrated during studies of complexation between tc and Mn^{2+} in solution [31]. Nevertheless, the presence of quadridentate or even terdentate bridging tc in the solid adducts herein studied can be ruled out. In fact, if only one of the two tc ligands per metal ion was involved in bridging of the above type, yielding infinite $-(M-tc)_x$ chains, the coordination numbers imparted by the tc ligands alone (one terminal and one bridging) would

be six or five for quadri- or ter-dentate bridging tc, respectively. Since the new complexes contain also coordinated $-OClO_3$ ligands and the M^{2+} complexes are pentacoordinated, the presence of polymeric $-(M-tc)_x$ chains is not possible. Consequently, the formulation of the complexes as monomeric chelates of the $[M(tc)_2(OClO_3)_2]ClO_4$ (M = Cr, Fe) and $[M(tc)_2OClO_3]ClO_4$ (M = Mn, Fe, Co, Ni, Cu, Zn) types, involving MO_6 and MO_5 chromophores, respectively, is reasonable. The tc ligands act as bidentate chelating, binding via the amide group oxygen and one of the C–O oxygens. Among the C–O oxygens of tc (*i.e.* at C3, C6, C10, C12 and C12a), that at C3 is the most probable binding site in the new complexes [1, 2, 10, 11, 25, 31], since in combination with the amide group oxygen it forms the six-membered chelate ring **II** (the oxygen at C1 would

II
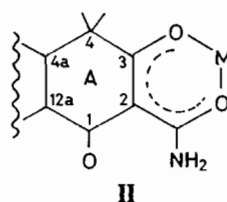
also form a similar chelate ring with the amide group oxygen, but is not involved in binding). Other potential second binding sites, such as the dimethyl-amino nitrogen at C4 and the oxygen at C12a are much less likely, since they would form seven-membered chelate rings in combination with the amide group oxygen. Regarding the conformation of the ligand in the new metal complexes, the NMR studies of Everett *et al.* [25, 31, 49, 50] have shown that the non-ionized form of tc (**I**) is converted to the zwitterionic form **III** in dimethyl sulfoxide (dmso)

III
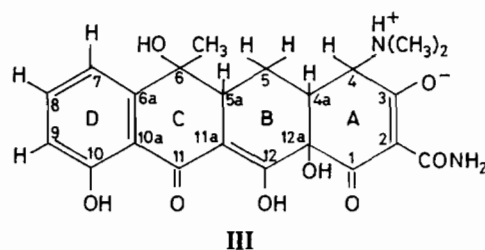
not only in the presence of H_2O or D_2O, but also of anhydrous metal salts such as $Mg(NO_3)_2$ [25]. The conversion of the non-ionized to the zwitterionic form of tc involves a conformational change from **IVA** to **IVB**, by rotation about the C12a–C4a bond [51]. Mg^{2+} in dmso displaces the **IVA** ⇌ **IVB** conformational equilibrium toward **IVB**, presumably by binding tc through two oxygens of the ring A tri-carbonylmethane in this conformation [25]. Among 3d metal ions, Mn^{2+} was found to coordinate to tc

IVA

IVB
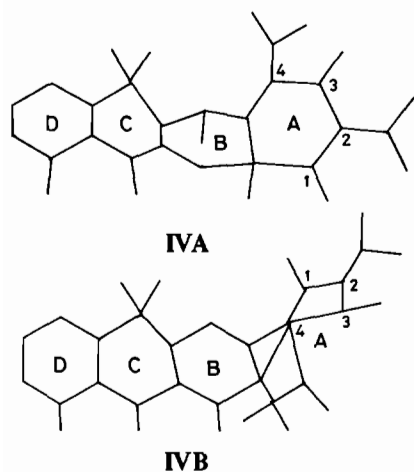
in conformation **IVB** by forming chelate rings with two oxygen sites of the ring A tricarbonylmethane and also the oxygens attached at C12 and C12a (chelation of a metal ion at C12O–C12aO is possible only in conformation **IVB**) [31]. In light of the preceding discussion, it is probable that chelating tc is in conformation **IVB** in the new metal perchlorate adducts under study.

References

1 C. M. Mikulski, J. Fleming, D. Fleming and N. M. Karayannis, *XXIV Int. Conf. on Coordination Chemistry*, Athens, Greece, Aug. 24–29, 1986, Abstract No D3 756.

2 C. M. Mikulski, J. Fleming, D. Fleming and N. M. Karayannis, *Inorg. Chim. Acta, 135*, L9 (1987).

3 D. L. J. Clive, *Q. Rev.*, 435 (1968).

4 W. Dürckheimer, *Angew. Chem., Int. Ed. Engl., 14*, 721 (1975).

5 M. Brion, L. Lambs and G. Berthon, *Inorg. Chim. Acta, 123*, 61 (1986), and refs. therein.

6 A. Albert, *Nature (London), 172*, 201 (1953); A. Albert and C. W. Rees, *Nature (London), 177*, 433 (1956).

7 J. T. Doluisio and A. N. Martin, *J. Med. Chem., 6*, 16; 20 (1963); J. L. Colaizi, A. M. Knevel and A. N. Martin, *J. Pharm. Sci., 54*, 1425 (1965).

8 E. C. Newman and C. W. Frank, *J. Pharm. Sci., 65*, 1728 (1976).

9 S. T. Day, W. G. Crouthamel, L. C. Martinelli and J. K. H. Ma, *J. Pharm. Sci., 67*, 1518 (1978).

10 W. A. Baker, Jr. and P. M. Brown, *J. Am. Chem. Soc., 88*, 1314 (1966).

11 B. Jeżowska-Trzebiatowska, J. O. Dziegielewski and P. Glowacki, *Bull. Acad. Pol. Sci., Ser. Sci. Chim., 27*, 223 (1979).

12 J.-C. Mani and G. Foltran, *Bull. Soc. Chim. Fr.*, 4141 (1971).

13 A. N. Speca, C. M. Mikulski, F. J. Iaconianni, L. L. Pytlewski and N. M. Karayannis, *Inorg. Chem., 19*, 3491 (1980).

14 N. M. Karayannis, L. L. Pytlewski and M. M. Labes, *Inorg. Chim. Acta, 3*, 415 (1969); N. M. Karayannis, C. M. Mikulski, M. J. Strocko, L. L. Pytlewski and M. M. Labes, *Inorg. Chim. Acta, 8*, 91 (1974).

15 C. Owens, J. M. Woods, A. K. Filo, L. L. Pytlewski, D. E.

Chasan and N. M. Karayannis, *Inorg. Chim. Acta, 37*, 89 (1979).

16 J. F. Coetzee and G. P. Cunningham, *J. Am. Chem. Soc., 87*, 2529 (1965); A. K. R. Unni, L. Elias and H. I. Schiff, *J. Phys. Chem., 67*, 1217 (1963).

17 W. J. Geary, *Coord. Chem. Rev., 7*, 81 (1971).

18 J. Reedijk, H. D. K. Codee and W. L. Groeneveld, *J. Inorg. Nucl. Chem., 35*, 1014 (1973).

19 D. E. Chasan, L. L. Pytlewski, C. Owens and N. M. Karayannis, *Ann. Chim. (Paris), 1*, 241 (1976).

20 H. Gehrke, G. Eastland, L. Haas and G. Carlson, *Inorg. Chem., 10*, 2328 (1971).

21 J. O. Dziegielewski, J. Hanuza and B. Jeżowska-Trzebiatowska, *Bull. Acad. Pol. Sci., Ser. Sci. Chim., 24*, 307 (1976).

22 A. Yamaguchi, T. Miyazawa, T. Shimanouchi and S. Mizushima, *Spectrochim. Acta, 10*, 170 (1957); T. Miyazawa, T. Shimanouchi and S. Mizushima, *J. Chem. Phys., 29*, 611 (1958); J. F. Baret, G. P. Carbone and J. Sturm, *J. Raman Spectrosc., 8*, 291 (1979); R. Savoie, J.-J. Jutier, L. Prizant and A. L. Beauchamp, *Spectrochim. Acta, Part A, 38*, 561 (1982).

23 J. J. Stezowski, *J. Am. Chem. Soc., 98*, 6012 (1976); R. Prewo and J. J. Stezowski, *J. Am. Chem. Soc., 99*, 1117 (1977).

24 C. R. Stephens, K. Murai, K. J. Brunnings and R. B. Woodward, *J. Am. Chem. Soc., 78*, 4155 (1956); G. O. Dudek and G. P. Volpp, *J. Org. Chem., 30*, 50 (1965).

25 G. W. Everett, Jr., J. Gulbis and J. Shaw, *J. Am. Chem. Soc., 104*, 445 (1982).

26 J. Donohue, J. D. Dunitz, K. N. Trueblood and M. S. Webster, *J. Am. Chem. Soc., 85*, 851 (1963).

27 N. E. Rigler, S. P. Bag, D. E. Leyden, J. L. Sudmeier and C. N. Reilly, *Anal. Chem., 37*, 872 (1965).

28 B. J. Hathaway and A. E. Underhill, *J. Chem. Soc.*, 3091 (1961); B. J. Hathaway, D. G. Holah and M. Hudson, *J. Chem. Soc.*, 4586 (1963).

29 R. B. Penland, S. Mizushima, C. Curran and J. V. Quagliano, *J. Am. Chem. Soc., 79*, 1575 (1957).

30 W. L. Driessen and W. L. Groeneveld, *Recl. Trav. Chim. Pays-Bas, 90*, 87 (1971).

31 J. Y. Lee and G. W. Everett, Jr., *J. Am. Chem. Soc., 103*, 5221 (1981).

32 A. E. Wickenden and R. A. Krause, *Inorg. Chem., 4*, 404 (1965); S. F. Pavkovic and D. W. Meek, *Inorg. Chem., 4*, 1091 (1965); M. E. Farago, J. M. James and V. C. G. Trew, *J. Chem. Soc., A*, 820 (1967).

33 C. M. Mikulski, L. S. Gelfand, L. L. Pytlewski, J. S. Skryantz and N. M. Karayannis, *Inorg. Chim. Acta, 21*, 9 (1977); D. Knetsch, *Ph.D. Thesis*, Leyden University, Netherlands, 1976.

34 G. Mann, H. Olapinski, R. Ott and J. Weidlein, *Z. Anorg. Allg. Chem., 410*, 195 (1974).

35 R. W. Adams, R. L. Martin and G. Winter, *Aust. J. Chem., 20*, 773 (1967).

36 J. R. Ferraro and A. Walker, *J. Chem. Phys., 42*, 1273, 1278 (1965).

37 C. M. Mikulski, M. K. Kurlan, S. Grossman, M. Bayne, M. Gaul and N. M. Karayannis, *J. Coord. Chem., 15*, 347 (1987).

38 B. B. Kedzia, P. X. Armendarez and K. Nakamoto, *J. Inorg. Nucl. Chem., 30*, 849 (1968).

39 M. Mikami, I. Nakagawa and T. Shimanouchi, *Spectrochim. Acta, Part A, 23*, 1037 (1967).

40 B. N. Figgis and J. Lewis, *Prog. Inorg. Chem., 6*, 37 (1964).

41 L. Sacconi, *J. Chem. Soc. A*, 248 (1970).

42 A. M. Brodie, S. H. Hunter, G. A. Rodley and C. J. Wilkins, *Inorg. Chim. Acta, 2*, 195 (1968); A. M. Brodie, J. E. Douglas and C. J. Wilkins, *J. Chem. Soc. A*, 1931 (1969).

43 C. M. Mikulski, J. Unruh, L. L. Pytlewski and N. M. Karayannis, *Transition Met. Chem.*, *4*, 98 (1979).
44 E. H. Gans and T. Higuchi, *J. Am. Pharm. Assoc.*, *46*, 458 (1957).
45 W. Byers, A. B. P. Lever and R. V. Parish, *Inorg. Chem.*, *7*, 1835 (1968).
46 L. Bèrtini, P. Dapporto, D. Gatteschi and A. Scozzafava, *Inorg. Chem.*, *14*, 1639 (1975).
47 M. Ciampolini and N. Nardi, *Inorg. Chem.*, *5*, 41, 1150 (1966); *6*, 445 (1967).
48 M. Ciampolini and G. P. Speroni, *Inorg. Chem.*, *5*, 45 (1966).
49 D. E. Williamson and G. W. Everett, Jr., *J. Am. Chem. Soc.*, *97*, 2397 (1975).
50 J. Gulbis and G. W. Everett, Jr., *J. Am. Chem. Soc.*, *97*, 6248 (1975); *Tetrahedron*, *32*, 913 (1976); J. Gulbis, G. W. Everett, Jr. and C. W. Frank, *J. Am. Chem. Soc.*, *98*, 1280 (1976).
51 L. J. Hughes, J. J. Stezowski and R. E. Hughes, *J. Am. Chem. Soc.*, *101*, 7655 (1979).